PROGNOSIS AND ANTICOAGULANT PROPHYLAXIS AFTER CORONARY OCCLUSION

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THE outlook after myocardial infarction has usually been assessed by comparing results of treatment in a few score patients with a simultaneous control series. The relatively small numbers in clinical trials (and in a disorder of such variable course 100 must be regarded as small), may lead to chance results which are deceptive. In most of the trials unequivocal diagnostic criteria have been demanded, and these have usually been the characteristic features that have been recognised for the past thirty years. A positive diagnosis is almost irrefutable, and the only errors are those of omission (Paton 1957). The studies of Björck et al. (1958) do not support the idea that recent improvements in finesse of diagnosis have added patients with improved survival prospects. Before long-term anticoagulant therapy was introduced there were many studies on prognosis, and to neglect them would be "snobbish" (Björck 1960).

We begin by reviewing the more important of these follow-up studies to reveal the factors on which prognosis depends. We are not concerned with the vexed problem of immediate mortality in the acute phase (Morris et al. 1952), but with the survival prospects of those who have recovered from a single recognised acute infarction. Though we shall mention some studies which deal with first or subsequent infarctions, and some which include angina, these are mainly used to provide supporting data on certain aspects.

Wider appreciation of the methods of calculating life-tables has compelled the discarding of many older studies where survival was estimated on patients who had died, and the recalculation of others such as the data of Sigler (1951) who tabulated the dead and living separately. Other papers were discarded because of inadequate information on important influences such as age.

Factors Influencing Prognosis

The more important studies on prognosis are summarised in tables Ia, Ib, and Ic, and are illustrated in figs. 1 and 2. The studies on myocardial infarction total 5398 patients, while the series including angina adds another 8639. While five-year survival tends to cluster round 65–70%, it will be shown that survival is much better in younger patients who have made a good recovery and worsens with increasing age in those with extensive lesions, and with complicating conditions like hypertension and diabetes.

Age and Sex

There is a striking difference between survival prospects in Waldron and Constable's (1950) series and those of Eckerström (1951): the average age in the former was 51·5, but the average age (66·7) of the latter series was obviously weighted by a substantial number in the eighth decade or over. Inspection of table I shows a general trend to higher five-year mortality

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TABLE Ia—PROGNOSIS AFTER SURVIVAL FROM THE FIRST MYOCARDIAL INFARCTION

Author	Patients		Start of follow-up	Percentage survival									
	Number	Mean age		1	2	3	4	5	6	7	8	9	10 (years)
Morris et al. (1952)	123	54	1 month	96	..	90	..	83	..	..	..	..	..
Robb and Marks (1953)	166	51·5	Disability benefit	93	84	81	76	70	67	63	58	54	53
Smith (1953)	85	..	2 months	88	..	71	..	64	..	..	..	..	53
Cole et al (1954)	285	57	2 months	..	..	..	..	67	..	..	..	..	44
Weiss (1956)	211	58	2 months	92	84	75	68	60	54	48	44	40	37
Helander and Levander (1959)	232	57	End of 1st admission	..	..	..	..	58	..	..	..	..	..
Beard et al. (1960)	427	53	2 months	92	86	79	73	69	..	..	..	..	..
Juergens et al (1960)	235	62	1 month	..	..	69	..	55	..	..	..	..	29

TABLE Ib—PROGNOSIS AFTER SURVIVAL FROM FIRST OR SUBSEQUENT INFARCTION

Author	Patients		Start of follow-up	Percentage survival									
	Number	Mean age		1	2	3	4	5	6	7	8	9	10 (years)
Eckerström (1951)	109	66·7	1 month	67	51	41	36	30	..	..	..	..	..
Waldron and Constable (1950)	1551	53	3 months	91	84	..	..	69	..	..	..	..	55
Olsen et al. (1956)	126	63	2 months	84	..	..	..	54	..	..	..	..	18
Richards et al. (1956)	162	56·7	1 month	..	..	..	..	49	..	..	..	..	31
Westlund and Hougen (1956)	929	63·1	1 month	80	60	55	..	..	..	..	..	..	..
Honey and Truelove (1957)	348	59	2 months	86	76	70	65	61	53	41	38	32	32
Björck et al. (1958)	246	63	End of 1st admission	83	76	69	63	59	..	50	..	..	40

TABLE Ic—PROGNOSIS IN PATIENTS WITH ANGINA PECTORIS OR INFARCTION

Author	Patients		Type	Start of follow-up	Percentage survival					
	Number	Mean age			1	2	3	4	5	10 (years)
Sigler (1951)	1147	55·8	Angina and infarction	Diagnosis	91	86	82	79	77	..
Block et al. (1952)	6882	58·8	Angina and infarction	2 years after diagnosis	84	..	70	..	58	37
Seim (1960)	610	59·6	Angina	Diagnosis of angina	92	88	83	79	74	..

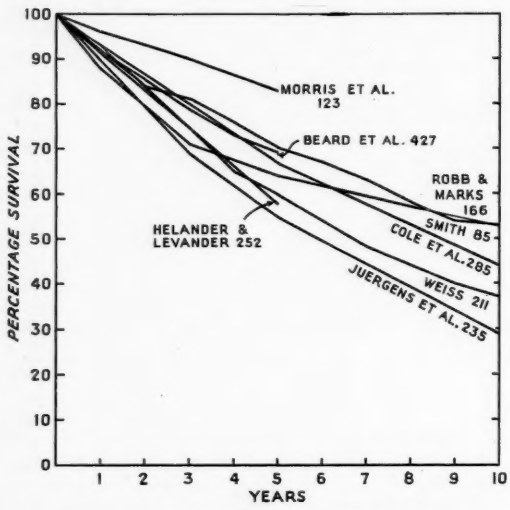

Fig. 1—Survival after first infarction in 1784 untreated patients.

The pattern of survival is remarkably similar in these patients: at five years it is about 65%. The lowest prognostic "line" included older patients.

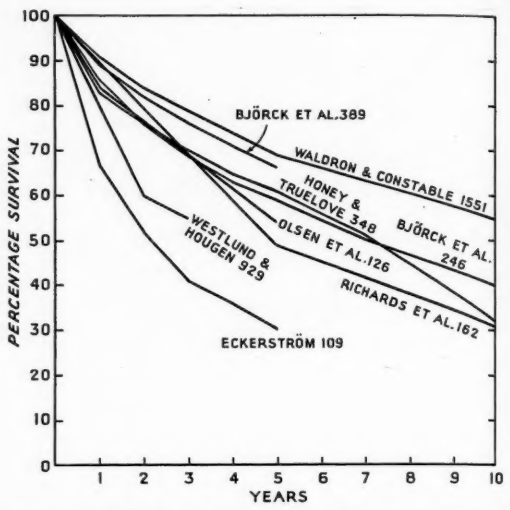

Fig. 2—Survival after first or subsequent infarction in 3614 untreated patients.

There is a wide spread of survival figures due to the types of patient studied. The upper ranges of survival to ten years are similar to those in fig. 1. The lower two series were older patients.

as the age of the patients advances (fig. 3), and the declining survival prospect with increasing age is also brought out by Block et al. (1952). Björck et al. (1958) hold that serious infarctions are more frequent in older patients, and in this they are supported by Helander and Levander (1959). In patients under 60, there is an invariable dominant incidence in men, but after 60 the sex-incidence becomes more nearly equal (Cole et al. 1954, Eckerström 1951). This may also account in part for the poorer survival prospects in women noted by Juergens et al. (1960). Although younger patients may survive longer, their life expectancy is more seriously shortened as seen from mortality ratios (deaths/expected deaths)—e.g., Björck et al. 1958.

Severity of the Attack

Russek and Zohman (1954) showed that the following features are additive in worsening prognosis: previous infarction, intractable pain, "shock", enlarged heart, gallop rhythm, congestive heart-failure, irregularities (especially atrial fibrillation or flutter), intraventricular block or ventricular tachycardia, diabetic acidosis, obesity, and pulmonary embolism. These features, particularly congestive failure, especially influence mortality in the first two years (Honey and Truelove 1957, Waldron and Constable 1950, White et al. 1960) (figs. 4 and 5). Electrocardiograms are not always helpful in assessing prognosis, though, naturally, a normal record is a good sign; Block et al. (1952) list certain changes, including the irregularities already mentioned, likely to be associated with a bad prognosis. Smith (1953) said that low voltage in the limb leads was an unfavourable sign. These electrocardiographic indications are only relative, and there are many exceptions (Helander and Levander 1959).

Degree of Recovery

Of patients who were symptom-free after infarction, 83% of 981 patients (Waldron and Constable 1950) and 82% of 55 patients (Richards et al. 1956) survived five years. Master et al. (1954) reported 9 deaths in the first quinquennium in 209 symptom-free patients, 138 of whom had already survived beyond five years—a death-rate of only 5% in this period. In a similar group, Cole et al. (1954) reported a 71% *ten*-year survival. Weiss and Weiss (1958) also showed that there was a much improved expectation of life in those who could return to work. Master's series brought out the progressive decrease in survival with increasing severity of angina and dyspnœa.

The prognostic significance of postinfarction cardiac pain may be difficult to judge, pain being such a subjective affair. Waldron and Constable even note an increased survival in patients with angina, but as their patients were receiving disability insurance benefits they may have had an interest in prolonging their pensions! Most physicians would agree with Smith (1953) who found that survival-rate was doubled in pain-free patients. Helander and Levander found that 65% of the patients able to return to work had some cardiac pain.

Diabetes, Obesity, and Hypertension

Bradley and Bryfogle (1956) reported a five-year survival of only 40% in their diabetics with myocardial infarction (mean age 60), and Björck et al. (1958) and other workers (fig. 6) reported a shortened survival-prospect in diabetic patients, only partly accounted for by the later age of development of this complication.

Though Russek and Zohman included obesity as a "poor risk" factor in the acute phase of infarction, there is no

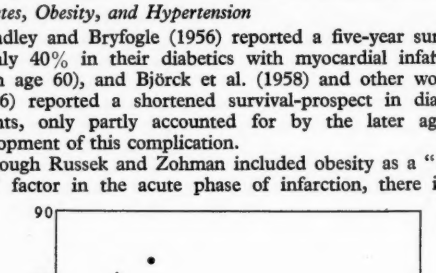

Fig. 3—The influence of average age upon survival at five years (from tables Ia and Ib).

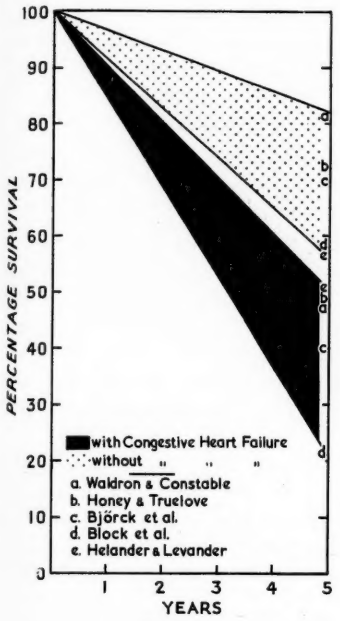

Fig. 4.

Fig. 4—Congestive heart-failure and survival.
This shows clearly that five-year survival is reduced if a patient has congestive heart-failure during the acute infarction (the intermediate years to five have been omitted).

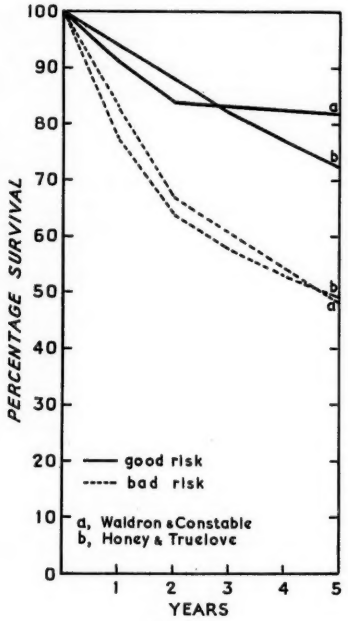

Fig. 5.

Fig. 5—Five-year survival of good-risk and bad-risk patients.
The five-year difference is clearly seen from the series of Waldron and Constable (1950) and Honey and Truelove (1957). Mortality is shown to be greatest in the poor-risk patients during the first two years after survival from infarction, but thereafter the mortality-rate is similar between good-risk and bad-risk patients.

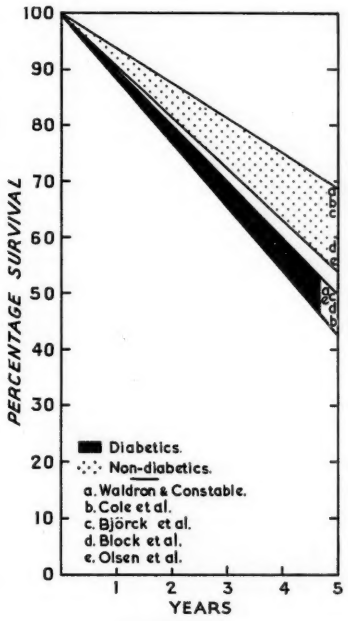

Fig. 6.

Fig. 6—The effect of diabetes upon survival at five years.
This diagram shows that the five-year survival is less in diabetics than in non-diabetics (intermediate years to five omitted).

evidence that it affects adversely the long-term prognosis (Bjerkelund 1957, Eckerström 1951) while Block et al. (1952) even noted an improved five-year survival in their obese patients! If this is correct, Lew's (1957) report of increased case-mortality in the obese would require some explanation other than coronary occlusion.

Juergens et al. (1960) found that the five-year survival of their hypertensives (blood-pressure 150/90 mm. Hg) was only 41% against 67% of those without hypertension: Waldron and Constable gave 60% and 82% respectively. The series of Björck et al. (1958), however, does not bring out this difference. Block et al. suggest that the worst prognosis is more closely related to cardiac enlargement and the severity of retinal changes (fig. 7).

Social Status

The best prognostic group reported was that of Morris et al. (1952) who had an 83% five-year survival in 123 doctors who had survived for more than one month after an acute infarction. No doubt they can take greater care of themselves and avoid undue physical strain.

Recurrent Myocardial Infarction

Major difficulties in the recognition of recurrent infarction are appreciated by most workers, especially in the presence of an already abnormal electrocardiogram: prolonged cardiac pain may occur without further changes. Sudden death is often ascribed to a recurrence, but the extensive necropsy records of Juergens et al. tabulated recurrent infarction (34%) and sudden death (27%) separately (see table II).

The incidence of alleged recurrence is greatest in the first or second year (Katz et al. 1949, Smith et al. 1942), the former authors stating that 56% of fatal recurrences occur in the first year, though Cole et al. (1954) report a declining incidence of recurrences as the years go by, and also a progressively decreasing immediate mortality.

If it is accepted that sudden death may result from such causes as ventricular fibrillation, independently of further occlusion, the omission of sudden death from any analysis probably means a corresponding inflation of numbers ascribed to recurrent infarction. Possibly less than half the fatalities result from recurrent infarction and a quarter are due to congestive cardiac failure (table II).

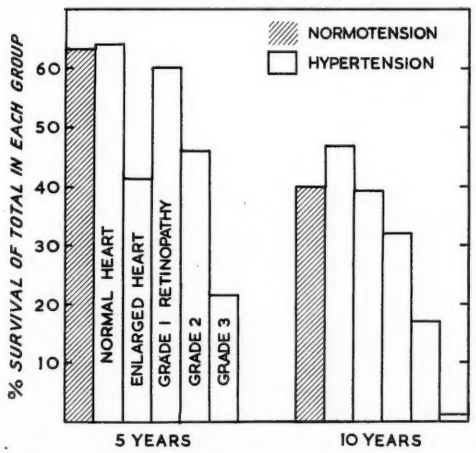

Fig. 7—The effect of hypertension upon survival at five and ten years (after Block et al. 1952).
The effect of advancing retinopathy upon survival at five years is evident; an enlarged heart affects survival considerably at five years but less at ten. The patients studied had angina pectoris and/or cardiac infarction. (Open rectangles at 10 years arranged as 5 years.)

TABLE II—CAUSES OF DEATH

Author	Total deaths in series	Causes of death—as percentage of total in each series				
		Recurrent infarction	Sudden death	Congestive heart-failure	Cerebrovascular accident	Other
Levine and Rosenbaum (1941) ..	80	40	35	20	..	5
Katz et al. (1949) ..	52	65·4	..	19·2	..	15·4
Sigler (1951) ..	393	56	14	13	5	12
Cole et al. (1954) ..	171	55	..	17	7	21
Olsen et al. (1956) ..	87	31	17·5	20·5	..	31
Richards et al. (1956)	160	51*	..	25	..	24
Weiss (1956) ..	142	38·7	19	23·3	7	12
Honey and Truelove (1957) ..	107	45	..	33·5	..	21·5
Björck et al. (1958)	489	42	..	32†	7	19
Juergens et al. (1960)	82	34	27	21	7	11
Seim (1960) ..	372	26	15	23	13	23

* This figure applies to cases described as " coronary insufficiency ".
† This figure applies to all cases of coronary heart-disease without evidence of acute infarction.

These studies show that the chances of survival following acute infarction can be assessed by consideration of age, sex, economic status, severity of the attack and degree of recovery, and complicating diabetes or hypertension. The slightest degree of unintentional bias in the selection of patients for treatment and control groups could profoundly influence the results.

Anticoagulant Treatment

The use of dicoumarol and phenindione in the treatment of acute myocardial infarction has been followed by a significantly lower mortality during the acute phase. Wright et al. (1948) reported the results of the American Heart Association's trial which showed a 24% mortality in the control series compared with a 15% mortality in the treated. In patients under 60 the crude death-rates were the same in both groups, but there was less non-fatal thromboembolism in the treated patients. They accordingly advocated the use of anticoagulants in the acute phase, especially in patients aged 60 and over. Feldman et al. (1952) studied 189 patients, and did not find that mortality was reduced, or that thromboemboli were less frequent in a series of treated and control patients matched for age, sex, and cardiovascular status. The work of Gilchrist and others in this country (Gilchrist and Tulloch 1956) has established a place for anticoagulant treatment in the acute phase, particularly to reduce thrombosis on the venous side, and subsequent emboli in the pulmonary and systemic circulations. That these are the effects of anticoagulants is postulated by Bjerkelund (1957), but he cautiously states that " one is hardly justified in concluding that this form of treatment also prevents arterial thrombosis, including coronary thrombosis itself, which in many respects is thought to be of a different nature and related to other pathogenetic factors ".

The claims of improvement in prognosis from acute-phase treatment have led to widespread interest in long-term treatment; but, in the absence of critical and controlled work, it is difficult to define the place of anticoagulants in preventing myocardial infarction. Gilchrist (1960) admits that in our present experience, and in the absence of all the desirable evidence, the case for long-term anticoagulant therapy amongst those with permanent myocardial damage is " not proven ", though the evidence in favour is very suggestive. Writing before the Medical Research Council (M.R.C.) (1959) report was published, Jordan and Punt (1958) suggested that " a study of the publications shows that—although the results are generally described as favourable—it is exceedingly difficult to use the figures given as a basis for a definite conclusion regarding this therapy ".

Control Series

We have shown that the prognosis for survival after recovery from myocardial infarction is influenced by many factors affecting the results of any trial unless critically matched in control and treated groups. Sometimes published results appear convincing until the control group is analysed. Bjerkelund (1957) and the M.R.C. (1959) studied patients who were matched accurately, but most other papers are less reliable.

Lack of an Adequate Control Group

Keyes et al. (1956) showed that mortality of their treated patients was 8·4% in four years compared with 41% in the same period in the untreated with first infarctions. No facts are given about the age, sex, or history of either the control or treated group, the former being two-and-a-half times as large as the group of 71 trated patients, suggesting some selection.

Tulloch and Wright (1954) studied a very small group (32 patients after the late phase of myocardial infarction) with a fifteen-month mortality of 6·2%, but they gave no facts about their patients, and so it is impossible to assess the results; and, in any case, this mortality does not differ significantly from the upper range of large untreated series (fig. 8).

Ensor and Peters (1959) used a " pseudo-control " group—i.e., a group of patients who had had anticoagulants for some time but who had discontinued treatment. The only fact given about the patients is the severity of the myocardial infarction in the treated group, but these authors are cautious in their claims as they only report a 79% five-year survival in treated patients against 70·7% in the " pseudo-controls ".

Nichol et al. (1958) studied the effect of anticoagulant treatment in patients with impending infarction, or in

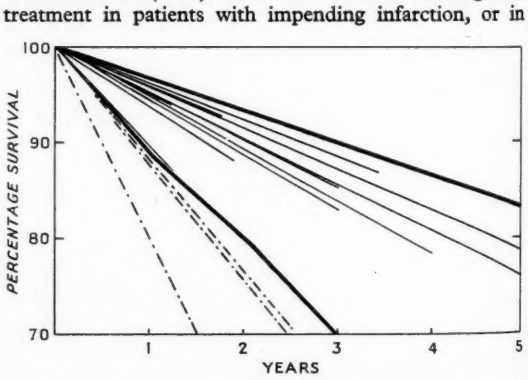

Fig. 8—Treated series compared with untreated.

The general prognosis derived from fig. 1 lies between the thick lines. The survival of treated patients (continuous lines) is shown using survival table data or percentage survival at the end of the average length of treatment. The treated series from above down are (1) Tandowsky (1959), (2) Muri (1956), (3) Ensor and Peters (1959), (4) Suzman (1959), (5) Ødegaard (1958), (6) Tulloch and Wright (1954), (7) Bjerkelund * (1957), (8) Waaler † (1957), (9) Nichol et al. (1958), and (10) Nichol and Bork (1950). The controls (dot-dash lines) from above down are those of Nichol et al. (1958), Bjerkelund (1957), and Suzman (1959). While the treated series tends slightly into the upper range of survival, the controls fare worse than usual.

* Based on total deaths. † Includes patients with angina.

those with one or two previous infarctions. They used as controls, however, patients from their records who had been previously followed up without any treatment. They also named a group of patients who abandoned long-term treatment. It is significant to note that 14% of the deaths in this group occurred within one month of stopping anticoagulants. But none of the groups were matched and the average period of follow-up differed in each. Their treated patients showed an 88% survival after an average period of 1·87 years, well within expectations of past experience (fig. 8).

Suzman et al. (1955) present formidable figures to show that patients on long-term treatment do better than those treated during the acute phase only. Although this is a careful study, the chief drawback to their results is that " the final decision for long-term treatment was left to the patient ". Economic factors obviously entered into the selection, and the results of treatment were a five-year survival of 76·1% against 45·6% in the untreated cases. Suzman (1959) has kindly allowed us to see his unpublished figures which show that recurrent infarction occurred only slightly less often (34·7% against 43·2%), but its mortality was less (40·5% against 74·8%) in long-term treatment patients than in the short-term group. These results, however, must be seen against the background of the selection of patients and the age-distribution of the groups; 31% of the patients in the short-term group were over 70, compared with only 20% in the long-term group.

Tandowsky (1959) does not mention his patients' status, except to describe the 70 controls as " a like group " in whom the mortality (53%) was four times that of the treated (13%); the average duration of treatment was three years and five months.

Use of Retrospective Studies to Provide Control Groups

Some papers which have given encouraging figures for survival in patients treated with long-term anticoagulants have not had a concurrent control series. Some writers have compared a series of patients treated in one country with a series reported in a different country some years before. Thus, Muri (1956) who had a 7·5% mortality at an average exposure to risk of twenty-one months compared his results with those of Parker et al. (1946) which were later included in the total series of Block et al. (1952), both reporting an exceptionally high (19 and 16% respectively) first-year mortality. Waaler (1957) who achieved a 17% three-year mortality, also used as controls the data of Block which are seen to be much worse than those of Sigler or Seim (table IC).

Tanzi and van Ness (1957) compared their mortality of 6·1%, in a sixteen-month average, with those " so far reported ". Toohey (1958), who had an 11·6% mortality at eighteen months, used as controls patients who had been followed up after myocardial infarction in the same and another hospital during the seven years before long-term anticoagulants: this series had a 33% two-year mortality. Toohey did not mention either age or sex among his patients, and so it is not easy to accept the claim that his results are " statistically significant ". His controls, who had a much higher mortality than usual, may have been an aged group; and his treated patients were not matched with the controls in any way.

Admission to Treated Group and Follow-up Care

Tanzi and van Ness (1957) and Keyes et al. (1956) limited their treatment to those who could cooperate. The former achieved 6·1% mortality in sixteen months while the latter had a 9·9% mortality between one and thirty-eight months of observation, results which lie within upper range of life expectation as shown in fig. 1. The striking five-year survival, 83%, which Morris et al. (1952) reported in medical practitioners, demonstrates the part played by intelligence, social status, and careful follow-up in survival after myocardial infarction. Constant supervision is certain to ensure earlier treatment of symptoms which may arise, and this is the only way in which the control group of patients in Bjerkelund's (1957) admirable study differed from the treated group. The latter were seen every one to three weeks against the three to four monthly intervals between the visits of control patients.

Results of Treatment

Although many reports have an inadequate control series, they give valuable facts about survival in the treated patients.

Survival of Patients

Many of the earlier papers included a few patients with myocardial infarction, and a larger series treated with long-term anticoagulants for thromboembolic disease, and so are not satisfactory for survival data. Tulloch and Wright's (1954) and Muri's (1956) figures have already been discussed. Nichol and Borg (1950) treated 78 patients for an average of fifteen months and reported a 15·3% mortality, which is less good than the average (fig. 8). Ødegaard (1958) treated 117 patients, of mean age 58·9 for a total of 343 patient-years, and found a mortality-rate of 4·87% per year—a little better than average but not outside the range of untreated patients. There was a 10% mortality in 735 patients with one infarction, studied for an average of twenty months by Nichol et al. (1958): they also reported an overall mortality rate of 12% in 1091 patients with impending one or two infarctions, studied for an average of 22·4 months. Both these figures are within " untreated " expectation. Manchester (1957) expresses his results as the fatality, and number of recurrent infarctions per 100 patient-years; these figures were 0·56 and 2·73 respectively. A survival table cannot be made from his data. He had twice as many patients with heart-failure requiring digitalis (33%) in his control group as in his treated group (15·6%). The five-year survival of 76% in Suzman's (1959) treated patients may well reflect the better social status of his patients.

The chief interest in the reports of Bjerkelund (1957) and the M.R.C. (1959) is the difference which is shown between the control and treated patients during the early months of long-term treatment. Bjerkelund (1957) stated that the " force of mortality " seemed to be largest initially in the control group, and that the treated patients—but only those under 60—did not show this initial excess mortality. It is noteworthy that in both Bjerkelund's and the M.R.C. series, most of the excess deaths in the controls took place in the first three months after infarction. Bjerkelund reported no statistical difference between the " force of mortality " in the treated and control group at any age, a year and more after infarction (see figs. 5 and 6 of his monograph). The M.R.C. trial showed a similar trend, and although 19 of the 28 deaths in the low-dosage group occurred in the first six months compared with only 9 of the 17 deaths in the high-dosage group " the difference in the death rate was appreciable only during the first three months of the follow-up period ". These results

are best demonstrated by the death-rates per 100 man-months of exposure during the first year:

Period	*Low dosage*	*High dosage*
Less than 3 months	2·7	0·8
3–6 months	1·7	1·1
6–9 months	0·8	0·5
9–12 months	0·0	0·8

While both these reliable reports show similar results, the efficacy of anticoagulant drugs was only transient. Suzman (1959) and Manchester (1957), however, report sustained improvement of prognosis, and so these four important protagonists are far from agreement on the reasons for their advocacy of long-term treatment.

No reported series shows that anticoagulant treatment in any way affects the pattern of an increasing mortality with age, or benefits older patients. This is thoroughly borne out by Bjerkelund's (1957) results with his older (over 60) patients, whom treatment did not benefit. Similarly, the difference between the low-dosage and high-dosage groups of men aged 55 and over was less marked than that in men under 55, which itself did not reach the 5% level of significance (M.R.C. 1959).

These results, and those which have been given above, show that it is probably only in the acute and healing phases of myocardial infarction that anticoagulant treatment may be effective in increasing survival, but even this is not yet statistically proven. Long-term anticoagulant prophylaxis beyond about two months after infarction cannot yet be justified by adequate evidence.

In small numbers of patients—and we must count the M.R.C. and Bjerkelund series as small—there are obviously possibilities of great variability indicated by "highly significant" results diminishing with the passage of time to statistical "insignificance" in both series. That chance could readily operate to account for the results is borne out by the recent work of MacMillan et al. (1960). In a statistically randomised series of 27 treated and 23 untreated patients, they had 8 deaths in the treated as against none in the untreated "controls".

Recurrence of Infarction During Treatment

The difficulties of establishing this diagnosis have already been mentioned, and the papers which report the results of treatment are not precise in defining the criteria for a recurrence. Bjerkelund (1957) alone classifies his patients into those with definite, very probable, and probable recurrences; and he points out that the diagnosis could not be established with equal certainty in all cases. However, the diagnosis of his recorded instances was definite in 63·5% of treated, and in 76% of untreated patients. He is careful to state that cases of sudden death were only included as recurrent infarcts if definite signs of a fresh infarct were found post mortem. Thus, his criteria differ from those of the M.R.C. report (1959) in which all cases of sudden death were attributed to recurrent infarction. Manchester (1957) does not mention the criteria for recognising a recurrence. These divergences explain the varying results of table III, where the incidence and mortality of recurrences in treated patients are shown. The apparent tendency towards a lower rate of reinfarction in the treated patients is open to critical doubt on account of the above difficulties of controls and diagnosis.

Certain facts must be emphasised which arise from this study of reinfarction. Bjerkelund (1957) makes a thorough study of the "force of recurrence" in his control group and shows a definite "excess of recurrences" in those under 60 during the first six months—but shows that this is not significant in the patients more than 60 years old. Moreover, after twelve months he can find no statistical difference between the "force of recurrence in the treated and control groups, and he finds that anticoagulant therapy has not given much protection to those with a high "force of recurrence"—i.e., those with a previous recurrent infarction. He claims that during the observation period two-fifths of the recurrent infarctions and at least half of the deaths due to recurrences were prevented by dicoumarol treatment. His most significant differences, however, were either in the first month of observation (i.e., near the acute phase) or in patients over 70.

The M.R.C. (1959) data on recurrent infarction differ from those of Bjerkelund in suggesting that a disparity in infarct-rate between high-dose and low-dose patients continues into the second year of follow-up. Although there were fewer cases of recurrent infarction among the treated, 17 out of 24 died from their recurrence, against 29 out of 60 in the low-dose group.

A reduced incidence of recurrent infarction in treated patients was also reported by Manchester (1957) and his results appear to be formidable evidence, but he did not give details of the patients studied, nor any criteria for the diagnosis of a recurrence. A large number (157) of his patients abandoned treatment, and these may have weighted survival in those continuing treatment towards a better prognosis, with fewer recurrences, as the M.R.C. report suggests.

Suzman (table III) also found a slightly lower rate of reinfarction in his long-term treated patients, especially in those whose previous infarction had been severe. However, the mortality of recurrent infarction was higher in the control group (49·4% against 27·6%). It is noteworthy that the mortality in Suzman's "treated" recurrences was about half that in the M.R.C. series where it was remarkably high (75%). Bjerkelund (1957) found that patients with a mild previous infarction had fewer recurrences, whereas Suzman (table III) found the reverse. Recommendation of long-term anticoagulants is thus based on widely divergent findings.

TABLE III—RECURRENT INFARCTION IN TRIALS OF TREATMENT

Author	Number of patients		Period of study (years)	Recurrence of infarction			
				Control		Treated	
	Control	Treated		Incidence (%)	Mortality (%)	Incidence (%)	Mortality (%)
Keyes et al. (1956)	234	121	2	38·0	..	2·0	..
Bjerkelund (1957)	118	119	3	40 (*a*)	44·6	22 (*a*)	34·6
Manchester (1957)	200	204	10	34	53·0	14·2	20·6
Nichol et al. (1958)	..	1091	1·87	..	..	10·75 (*b*)	66
Medical Research Council (1959) ..	188	195	3	27·5	46·5	12·3	75
Suzman (1959)	216 (*c*) mild	55	10	32·8	49·4	34·5	27·6
	298 (*c*) severe	115	10	50·7	61·4	34·8	38·3

(*a*) Includes cases classified as definite, very probable, and probable myocardial infarction.
(*b*) Includes cases described as ventricular fibrillation or cardiac arrest (i.e., sudden death).
(*c*) Refers to severity of first attack of infarction.

Return to Work

It has already been shown that many patients are able to return to work, and to stay at work after recovery from myocardial infarction without long-term treatment. It is disappointing, therefore, that Bjerkelund (1957) found that only slightly more treated than control patients returned to work. The small difference between the two groups probably depended upon more elderly patients among the controls. Bjerkelund states that the " difference hardly gives reason to believe that the treatment has influenced the patient's ability to work ". The M.R.C. (1959) found that there were slightly more men at work in the treated group (83% against 71%), but the proportion without dyspnœa was the same (66% and 67%). This is the more remarkable as the 31 of the " untreated " survivors had had an additional recurrent infarction. Muri (1956) reported that 79% of treated patients were at work, a figure in agreement with the M.R.C. treated and untreated groups, and thus hardly to be claimed as a therapeutic success.

A patient's return to work will in part be determined by his symptoms. A common symptom which can limit ability to work is cardiac pain, which has been reported to be less frequent in patients treated with anticoagulants. We wish, however, to repeat Bjerkelund's (1957) statement that " cases of angina pectoris often have spontaneous fluctuations, and this makes assessment of prophylactic therapy very difficult ".

Manchester (1957) found that 38 of 74 treated patients had less cardiac pain, compared with only 20 of 72 control patients. Similar figures were given by Tandowsky (1959) for the abatement of coronary insufficiency, and Waaler (1957) found that 38% of his series of treated patients with angina pectoris were wholly relieved, and 12% were partially relieved of pain. The M.R.C. (1959) reported that the absence of anginal pain suggested a slight superiority among the treated (64% against 52%) over three years of study. Bjerkelund (1957) meticulously subdivided his patients according to their grade of cardiac pain, but was not convinced that dicoumarol had any " definite " prophylactic effect against this symptom.

Thromboembolism

The prevention of venous thromboembolism after the initial acute phase does not receive much prominence in any report, and it is evident that it is not very important clinically after the acute phase, though when it is recognised, the mortality is high.

Manchester (1957) reported 35 cases (17·5%) of whom 16 (45·7%) died in his untreated group, against only 5·8% with a 14·2% mortality in his treated patients. Bjerkelund (1957) found extracardiac thromboemboli in only 2 of his control group, and in none of his treated group. Suzman (1959) found thromboembolism three times more frequently in his untreated patients. Only 1 case is mentioned with a fatal cerebral embolus in the M.R.C. low-dosage group. It seems likely that patients on anticoagulants are protected from venous thromboembolism (Sevitt and Gallagher 1959).

There is adequate postmortem evidence, however, that coronary arterial thrombosis can, and frequently does, develop in patients under expert anticoagulant control. Fresh coronary-artery thrombosis was found at necropsy in 58% of Bjerkelund's untreated patients, and, post mortem, in 26% of his treated patients. Capeci and Levy (1959) were not impressed by any diminution of thrombus formation in treated patients who came to necropsy.

Indications for Treatment

Two different opinions are held about choice of patients for, and duration of, treatment. Nichol and Fasset (1947) decided to use anticoagulants for patients with recurrent infarction. Wright et al. (1954) and Suzman et al. (1955) also reported that this type of patient might benefit from treatment. The M.R.C. (1959) found that a lowering of the infarction-rate appeared most clearly in those in whom the risk of recurrent infarction was high, in younger males, and in those with more than one infarct. On the other hand, Bjerkelund's results indicated that there was no benefit from treatment in patients who had had more than one infarct: he would recommend treating all, or a large number of, patients for six months or a year, but not thereafter. The M.R.C. report, however, recommends that " continuous " treatment should be given as this can make a useful, if limited, contribution in the aftercare of patients who have recovered from the acute phase of myocardial infarction, in spite of their own evidence that the regime is of little value after six months.

Discussion

At the beginning of this paper, we showed that patients who survive the acute phase of a myocardial infarction have a five-year survival-rate of about 66%. This figure has varied according to the type of patient who has been followed up ranging from above 80% in the doctors studied by Morris et al. (1952) to 30% in Eckerström's (1951) elderly patients. We have mentioned the remarkably good five-year survival figures for patients who make a complete clinical recovery, or who are young at the time of their infarction. All this evidence shows that myocardial infarction may often be followed by long survival. The various factors which affect prognosis have been documented in order to give a background of experience against which the results of long-term prophylaxis may be reviewed.

In studying the published reports on anticoagulant prophylaxis, we have become critical of the controls, who have often been at, or below, the lower extreme of prognosis found in untreated patients, while the treated fare no better than those in the upper range of survival prospect (fig. 8). The careful studies of Bjerkelund (1957) and of the M.R.C. (1959) have been a constant source of valuable data, but there is surprisingly little work of similar calibre in other studies.

Despite many claims, the evidence that long-term anticoagulants prevent recurrence, or reduce mortality, after the acute phase of infarction is still inadequate. Most of the benefits reported by Bjerkelund and by the M.R.C. working party occurred in the first few months —i.e., while patients were still recovering from the acute event. If the action of the drugs is to prevent arterial thrombosis, there is no reason why this prophylactic action should cease after a few months, and it may well be that the early benefits reported in the Bjerkelund and M.R.C. series are in fact related in some way to the early healing phase of the actual infarction. Another possibility is of harm to the controls from sudden termination of acute-phase treatment.

It seems possible that most of the benefits which have been reported in the acute phase of infarction are related to the efficacy of the drug in limiting venous thrombosis and preventing pulmonary embolism; most reports are consistent in this respect. The recent studies by Sevitt and Gallagher (1959) on prophylaxis of venous thrombosis with phenindione in patients with fractured femora are most encouraging. The apparent failure of the same measures to prevent coronary occlusion is all the more disappointing. Antiprothrombin drugs have also failed in cerebrovascular occlusive disease (Marshall and Shaw

1960), and in occlusive arterial disease of the legs (Singer and Rob 1960).

Venous and arterial thromboses probably differ considerably in their pathogenesis. Venous thrombosis is undoubtedly promoted by stagnation in veins of the calf, often subjected to prolonged mechanical pressure in bed in debilitated patients. Arterial thrombosis, on the other hand, is based on underlying disease of the arterial wall—atheromatous plaques and ulcers, which can liberate local tissue thromboplastins into the blood-stream, which in turn may be retarded by upstream narrowing of the vessel. Ischæmia and myocardial infarction have been reported in patients with hæmophilia (Boivin 1954, Borchgrevink 1959, Stewart and Acheson 1957). The development of arterial occlusions in these patients reinforces the importance of local release of thromboplastin from the damaged intima as a crucial event in the changes leading to thrombosis, even of hæmophilic blood (Astrup et al. 1959). Mural thrombi over infarcts form with almost equal frequency in patients on anticoagulants as compared with controls (Gilchrist and Tulloch 1956). Such observations raise serious doubts on the usefulness of anticoagulants in preventing local thrombosis on damaged arterial intima.

Any problematic benefit from anticoagulants in the prevention of thrombosis should be weighed against the considerable risk of hæmorrhage mentioned in most reports. Lethal cerebral hæmorrhage occurred in 4 out of 118 patients in Bjerkelund's (1957) series; 2, and possibly 3, fatalities were also recorded from Newcastle (Fuller 1959). Quite apart from the risk of cerebral and other fatal hæmorrhages, morbidity can result from serious bleeding from anticoagulant treatment. Anticoagulants may not avert arterial occlusion, and there is a real, and probably increased, risk of thrombosis in the period immediately after the drugs are stopped. Various reports have suggested that sudden cessation of antiprothrombin drugs may be followed by arterial occlusion within a short time (Nichol et al. 1958); 20 such instances are documented by Dinon and Vander Veer (1960). It is not impossible that this complication may have been responsible for the early high mortality, so near the end of acute-phase treatment, in both the M.R.C. and the Bjerkelund control patients. Hence, when anticoagulants have been used in the acute phase of myocardial infarction, their administration should be tapered off over a period of three to four weeks.

Finally, it is well to remember that factors other than thrombosis also play a part in the production of myocardial infarction. Among them are thickening of the atheromatous plaques themselves, subintimal hæmorrhage (Paterson 1936, Paterson et al. 1957), and sudden falls of blood-pressure reducing perfusion of critically narrowed coronary vessels. Furthermore, recurrent thrombosis may be responsible for a little more than half the ultimate death-rate in patients who have recovered from a cardiac infarction.

Summary

The survival of patients after recovery from myocardial infarction, and the factors which influence prognosis, have been studied from reported series.

There is broad agreement in the published data, totalling over 5000 patients (table Ia and Ib), that the prospect of five-year survival in cases under 60 ranges round 66%, being worse with increasing age and complications, and better with improving social circumstances and completeness of recovery.

Long-term anticoagulant prophylaxis, as carried out today, shows no evidence of improving life expectancy when compared with the prognosis in this large collection of " untreated " patients.

Possible reasons for this inefficacy of long-term anticoagulant prophylaxis are briefly discussed against the background of contrasting mechanisms of arterial and venous thrombosis. The possibility should also be considered that some of the early high mortality in " controls " may be the result of sudden cessation of " treatment ".

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POTASSIUM IN THE TREATMENT OF CHOLERA

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Sir Leonard Rogers, in 1909, advocated the use of a hypertonic solution containing sodium chloride, calcium chloride, and 0·4 g. (5·4 mEq.) per litre of potassium chloride, for the treatment of cholera; but in 1916 he decided to omit potassium from the mixture because "some physiologists consider it unnecessary and possibly harmful". In 1946, Govan and Darrow demonstrated a fivefold reduction in mortality from infantile diarrhœa when potassium was added to replacement solutions used parenterally. Electrolyte studies by the United States Navy in the 1947 Egyptian cholera epidemic showed an excessive loss of potassium in the stools; hence it was recommended that potassium 6·7 mEq. be included in each litre of intravenous solution used in the treatment of cholera (Johnson et al. 1948). Chakravarti and Chaudhuri, in 1954, recommended giving potassium salts, when the acute diarrhœa of cholera had subsided, to hasten convalescence, providing that renal function was satisfactory. Despite the above, a recent review of cholera therapy (Pollitzer 1957) does not mention the use of potassium in the treatment of the acute disease.

The Study

During the 1958 cholera epidemic in Bangkok, Thailand, seventeen patients with proven cholera were studied intensively during their acute illness. For the first 24 hours nothing was allowed by mouth in order to relate the fæcal changes to changes in plasma-electrolyte composition. Thus, during the first 24 hours, fluids were given exclusively by the intravenous route. Meanwhile balance studies were made, and afterwards a diet of boiled eggs, rice gruel, milk, and water was given ad libitum. The fæces and urine were collected and measured daily until the patient was discharged. A detailed report of this investigation, including methods and procedures, has been published (Watten et al. 1959). While it is impossible from these studies to calculate balance data for more than 24 hours after admission, approximate potassium losses during the 2–4 days of diarrhœa may be calculated.

TABLE I—MEAN HOURLY FÆCAL VOLUME AND ELECTROLYTE CONCENTRATION OF CHOLERA STOOLS COLLECTED OVER 24-HOURS

—	Volume (ml. per hr.)		Electrolytes (mEq. per l.)			
	Mean	Range	Na	Cl	K	HCO_3
11 patients with fæcal volume over 125 ml. per hr.	340	130–730	137	107	16·1	45·2
6 patients with fæcal volume under 125 ml. per hr.	100	23–120	114	89	26·4	43·5

Patients with severe cholera had 24-hour fæcal volumes of 3–17 litres. In these patients the total volume of diarrhœal fluid during the 2–4 days of the disease was 10–35 litres. During the 24-hour balance period, the mean potassium content of the fæces was 16 mEq. per litre (table I), and potassium losses in fæces and urine averaged 158 mEq., with a range of 50–245 mEq. The total fæcal and urinary loss of potassium for the entire period of diarrhœa varied from 400 to 700 mEq.; or, for a 50 kg. man, the loss was 15–30% of the total exchangeable body-potassium, assuming this value to be 49 mEq. per kg. body-weight for a normal man (Edelman and Leibman 1959).

Fæcal potassium concentrations vary inversely with fæcal volume (Watten et al. 1959). Table I shows that patients with fæcal volumes in excess of 3 litres per day (125 ml. per hour), had fæcal sodium and chloride concentrations which were nearly isotonic with those of the plasma, while the potassium and bicarbonate concentrations were higher than the plasma levels.

With amelioration of diarrhœa and decrease in fæcal volume, the potassium concentration increased while the sodium concentration decreased; this is related to selective reabsorption of sodium in exchange for potassium in the lower ileum and large bowel, and it has been demonstrated experimentally by D'Agostino et al. (1953). Paralytic ileus, with abdominal swelling and cessation of diarrhœa, was often seen in patients whom we studied during the 1958 Bangkok cholera epidemic.

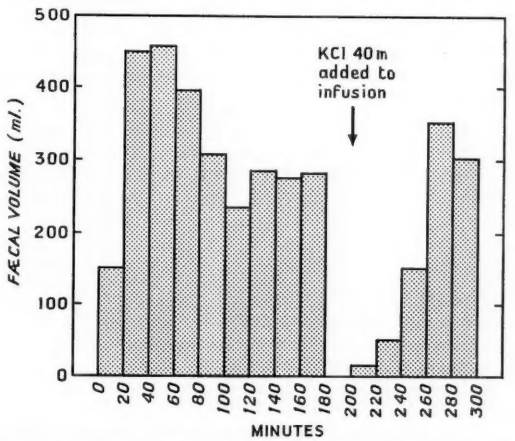

Fig. 1—Fæcal volume measured at 20-min. intervals during constant infusion (15 ml. per min.) of normal saline (4-140 min.) and 2% sodium bicarbonate (140-240 min.).

This complication, as Wilkinson (1943) pointed out, is probably responsible for the rare examples of so-called cholera sicca, in which death results from massive transfer of fluid into the bowel lumen without diarrhœa.

Fig. 1 shows 20-minute fæcal volumes in a patient during infusions of normal saline and 2% bicarbonate solution. The drop in fæcal volume at 180 minutes was probably the result of potassium deficiency, because balances at that time revealed a loss of 165 mEq. of potassium. Fæcal volume increased after infusion of 40 mEq. of potassium chloride, and then it remained constant with additional infusions of potassium. The sequestration of a large volume of diarrhœal fluid in the bowel, caused by paralytic ileus, can be misleading and dangerous if fluid therapy is based on replacement of observed fæcal volume alone. Utilisation of more accurate measurements of dehydration, such as plasma-specific-gravity determinations (Phillips et al. 1950) will prevent such errors.

During our cholera studies, alkalosis developed after treatment in four patients who had been given only 20–80 mEq. of potassium (replacing about 10% of the deficit) during treatment (table II). The plasma-CO_2 content remained above 30 mEq. per litre for as long as 7 days after the diarrhœa

TABLE II—ADMISSION AND CONVALESCENT PLASMA-CO_2 CONTENT AND POTASSIUM LEVELS IN FOUR PATIENTS WITH SEVERE CHOLERA

Patient no.	24-hr. fæcal volume (ml. per hr.)	Plasma-CO_2 content (mEq. per l. plasma-water)		Plasma-potassium (mEq. per l. plasma-water)		Interval (days)
		Admission	Convalescent	Admission	Convalescent	
2	476	22·2	29·3	4·5	3·8	7
10	235	14·0	37·0	4·8	3·3	6
12	302	11·1	30·4	4·3	3·1	3
15	725	20·5	33·3	4·9	3·4	7

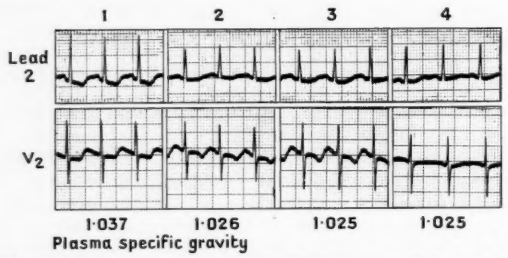

Fig. 2—Patient no. 6, 30-year-old Thai woman, 24-hour fæcal volume 7700 ml.

The tracings were made: (1) on admission at 12.30 P.M. (plasma-CO_2 content 15 mEq. per litre); (2) at 2 P.M. after rehydration with 3 litres of normal saline; (3) at 4.30 P.M. after infusion of 500 ml. of 2% sodium-bicarbonate solution (which raised the plasma-CO_2 content to 22 mEq. per litre; and (4) at 5.30 P.M. after infusion of 40 mEq. of potassium chloride in 1 litre of normal saline.

ceased, despite a normal diet. The data were not complete enough to indicate the pathogenesis of alkalosis associated with potassium deficiency in cholera, but they do indicate that a moderate alkalosis developed in several patients with serious potassium depletion, who had been treated with adequate quantities of saline and bicarbonate.

Serial electrocardiograms were taken during treatment of thirteen patients, but only five showed definite evidence of potassium deficiency either before or after the dehydration had been corrected with saline. Fig. 2 shows the changes in a patient with severe cholera. During the 5 hours before admission this patient passed seven watery stools, and was moderately dehydrated. The first tracing, taken 6 hours after the onset of the patient's diarrhœa, showed T-wave alterations in all leads. T-wave changes were less pronounced after saline and bicarbonate infusions, but they did not return to normal until potassium had been given. These changes were not caused by dehydration because plasma-specific-gravity values were within the normal range during the infusion therapy.

Discussion

Rational treatment of cholera requires knowledge of the altered physiology and chemistry of this disease. Such information has not been available until recently (Watten et al. 1959), and consequently therapeutic regimens have changed little since Rogers' recommendations of 50 years ago. There is universal agreement on the necessity for prompt replacement of water and salt, and the use of bicarbonate for the treatment of acidosis is accepted; but the risk of pulmonary œdema from overhydration (Chaudhuri 1950, Chakravarti and Chaudhuri 1954) is emphasised far more often than the danger of insufficient fluid replacement. Myocardial depression caused by potassium depletion rather than by rapid replacement of fluid may well be the important factor in the genesis of this complication. Death from "heart-failure" during convalescence (Baligh 1948) may also be due to deficit of potassium. Moreover, adjuvants to therapy (colloid plasma-volume expanders, cardiac stimulants, vaso-pressor agents, bacteriophage, antibiotics, &c.) continue to be given emphasis out of proportion to their value, and they detract from what should be the main line of cholera therapy—i.e., replacement of the lost water and electrolytes.

A lesser-known result of potassium depletion is renal tubular damage; vacuolisation of distal tubular cells, and damage to the collecting tubules, have been reported (Relman and Schwartz 1958, Holliday 1959). In a recent study of patients dying in uræmia after cholera, Benyajati et al. (1960) found microscopic changes in renal structure similar to those produced by potassium depletion. Ischæmic renal damage and uræmia due to delayed or inadequate fluid replacement is a frequent complication of cholera. Damage to kidney structure and impairment of function produced by potassium loss may contribute to renal failure in these cases.

Neuromuscular disturbances are a well-known complication of potassium deficiency. But there is only one report of transient potassium-depletion paralysis following cholera in eleven convalescent patients; this promptly subsided after potassium-chloride infusions had been given (Huang and Mao 1947). Instances are known of "secondary collapse" involving weakness, muscular twitching, and tetany during convalescence from cholera (Dr. C. Benyajati, personal communication).

Although plasma-potassium levels will eventually reflect potassium deficits, determinations made during the acute phase of cholera are of no value in establishing the need for potassium replacement. Data from our studies (Watten et al. 1957) indicate that plasma-potassium levels in acutely dehydrated patients were within the range of normal when corrected for plasma-protein concentration (expressed as mEq. per litre plasma-water). Furthermore, plasma-potassium values after rehydration were also within the range of normal. These findings indicate, as Scribner et al. (1958) concluded, that plasma-potassium concentration is independent of the volume of the extracellular space.

Saline solutions have been the foundation of cholera treatment. Table I shows that, for each litre of fæces lost from a patient with severe cholera, a litre of approximately isotonic saline will replace the salt lost. Theoretically, each litre of replacement solution should also contain about 16 mEq. of potassium and 45 mEq. of bicarbonate to replace these electrolytes.

The amount of potassium required to replace the deficits in acute cholera should be sufficient to prevent complications without producing toxicity. Ideally, measured potassium losses in urine and fæces would be exactly replaced; but facilities for this are rarely available in areas where cholera remains a problem, and even if they were the demands on time, personnel, and the laboratory during an epidemic would preclude their use except in the exceptional patient.

It therefore seems advantageous to add a small amount of potassium to each bottle of replacement solution. But the rapid infusion of 3–4 litres of a potassium-containing solution during the initial treatment of shock and collapse might increase the plasma-potassium levels too much, with the danger of heart-block and other conduction defects. Until further information is available it is advisable to use parenteral potassium only after the initial dehydration has been treated, and when maintenance solutions are given more slowly.

For the treatment of potassium depletion in infantile diarrhœa, Govan and Darrow (1946) recommended a solution containing 35 mEq. of potassium per litre which he never gave at the rate of more than 120 ml. per hour. In adults, Nadler et al. (1950) reported no untoward effects in treating the potassium depletion of diabetic acidosis and prolonged vomiting with an isotonic solution of potassium chloride (155 mEq. per litre) given intravenously at a rate of 290 ml. per hour (45 mEq. potassium per hour). But these infusion rates are far less than we have found necessary to maintain hydration in cholera patients; and an infusion-rate of 100 ml. per minute is

necessary for the rapid treatment of collapse during the initial period of rehydration.

Without electrocardiographic or laboratory control, which is impossible during the treatment of large numbers of acutely ill cholera patients, a solution is needed that is safe under a variety of conditions. The addition of 10 mEq. (7·5 g.) of potassium chloride to 1 litre of saline should satisfy this need, and during an epidemic this solution could be used with safety in remote areas, even without medical supervision. It will replace at least half the initial potassium deficit in the average severe case, and it should prevent the major complications of potassium deficiency. As long as diarrhœa continues 10 mEq. potassium may be added to each litre of maintenance solution with impunity, even when the renal function is unknown, because potassium will continue to be lost in concentrations of 10–50 mEq. per litre of fæces (Watten et al. 1959). With cessation of diarrhœa, if renal function is not satisfactory, potassium should be discontinued. In uncomplicated cases, 10 ml. of a palatable mixture containing 100 g. each of potassium citrate, potassium acetate, and potassium bicarbonate per litre of water may be diluted and given by mouth three times a day as soon as nausea and vomiting cease.

From the electrolyte data reported in this paper, and from knowledge of experimental and clinical potassium depletion, one can conclude that the recommended addition of potassium should provide a more physiological approach to cholera therapy, diminish complications, and further reduce the mortality-rate.

The opinions and assertions contained herein are those of the authors, and they are not to be construed as official or as reflecting the views of the Navy Department or the Naval Service at large.

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". . . One of the explanations why people in general are rather well satisfied by living and working in these regulated national communities of the Western World is undoubtedly that they do not notice the controls so much, or do not react so violently, as they are becoming accustomed to them. The present level of taxation in all Western countries, for instance, would have been unthinkable fifty or even twenty years ago. There is a deep truth in Albert Einstein's observation, that if there were beings who were flat and without thickness, and who lived on the surface of a sphere, they would have no idea of a third dimension. Like domesticated animals, people growing up in the Western type of regulated national communities have no real conception any longer of a wilder life. To the reflecting social scientist the adaptability of the human animal to new conditions will never cease to be one of this world's wonders."
—GUNNAR MYRDAL. *Beyond the Welfare State.* London, 1960.

FALLACIES IN INTERPRETATION OF QUECKENSTEDT'S TEST

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IN 1916 Queckenstedt introduced his test for the detection of spinal subarachnoid obstruction. He noted that compression of the jugular veins caused a " congestion of the brain ", and consequent increase in the cerebrospinal-fluid (C.S.F.) pressure. In the presence of an expanding spinal lesion sufficient to block the subarachnoid space, this increase is not transmitted to the spinal canal, and is therefore not reflected in the fluid level of a lumbar manometer. Queckenstedt wrote of congestion of the brain. Had this conception been retained, and not replaced, as it was, by that of increased intraventricular pressure, later confusion might have been avoided. As the original test was modified, and combined cisternal and spinal puncture methods were introduced to define the site of obstruction more precisely, inaccuracies in the interpretation of results appeared.

The first refinement was added by Ayer (1921), who, having perfected his technique of cisternal puncture, used it in combination with lumbar puncture to show a rise in cisternal pressure without a coincident lumbar increase as additional evidence of spinal obstruction.

About 1924, at least three workers—Fremont-Smith, Cushing, and Eskuchen—independently described a method of combining ventricular with lumbar puncture to confirm the diagnosis of posterior-fossa obstruction; but here conditions are dissimilar to those in the spinal theca, and the test thereby becomes less reliable.

Further improvements in detail were added. Poppen and Hurxthal (1934) pointed out that before evidence of block is manometrically apparent, the subarachnoid obstruction must develop to a degree in which the area left for fluid circulation is less than the area of cross-section of the spinal-puncture needle. Stookey and Klenke (1928) placed the test on a firmer mathematical and mechanical basis by explaining the delayed rise and the rise maintained after removal of jugular compression. Grant and Cone (1934) applied graduated pressures to the neck by a manometer cuff in steps of 5 and 10 mm. Hg and recorded them, with successive C.S.F.-pressure readings, on a chart. This obviated the individual variants of degree and site of finger compression, and gave comparable records compiled by different observers.

Antoni (1931), at the Copenhagen clinic, modified the combined cisternal and spinal test. He postulated that, as the superior caval venous pressure decreased with the inspiratory expansion of the thoracic cage, and the inferior caval venous pressure increased with the descent of the diaphragm, the cisternal level should fall and the lumbar pressure rise with each inspiration, if a block existed between the needles. Wagner (1947), reporting over 800 double punctures from the same clinic, concluded that the test for " respiratory block " was not reliable, because the communicating vertebral venous system equalised the pressure between the superior and inferior caval systems.

In the " reversed Queckenstedt test " saline is injected into the sacral epidural space, raising the pressure at that level. The absence of a corresponding rise at a higher lumbar site signifies subarachnoid obstruction between the two needles.

As a result of these combined methods, many observers, instead of thinking in terms of venous distension causing increased pressure, thought instead of columns of C.S.F. moving from one part of the cerebrospinal axis to another. For example, Elsberg (1941) said: " The compression of the jugular veins causes a venous congestion within the cranial cavity, and as a result, the expulsion of C.S.F. from

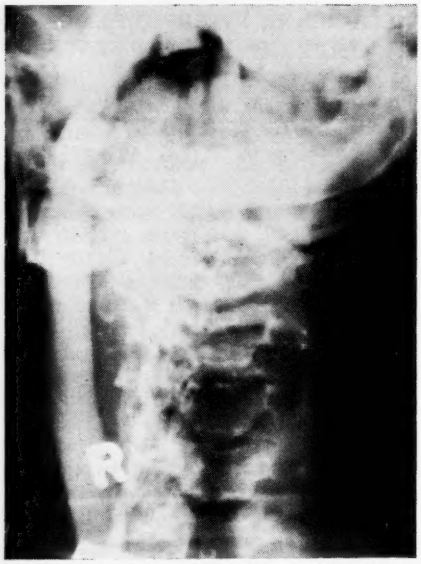

Fig. 1—Injection into the internal jugular vein of a living subject with both jugular veins compressed.

Contrast medium is seen filling the vertebral venous systems of the same side as far as the lower cervical region.

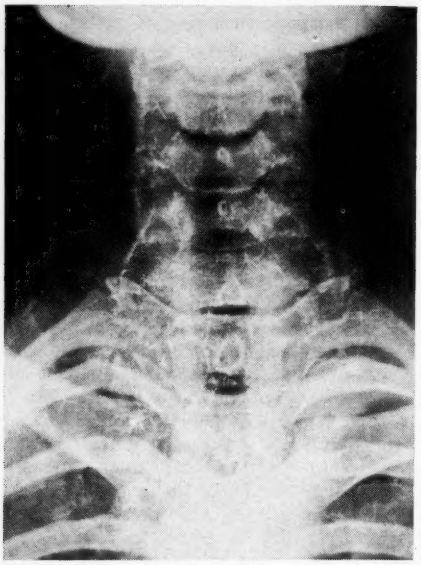

Fig. 2—Injection into the jugular bulb in a cadaver with jugular veins compressed.

The vertebral venous system is filled on both sides to the lower cervical level.

the ventricular cavities." This misconception of rising ventricular pressure was encouraged by Dandy and Blackfan's (1914) theory that the rise in C.S.F. pressure was caused by congestion of the choroid plexuses and increased fluid production in the ventricles. Becht (1920) disproved this by showing that C.S.F. pressure returned to its initial level within 11 seconds after release of jugular compression, but took 6 minutes to return after the volume of C.S.F. was increased by the subarachnoid injection of saline.

That venous and C.S.F. pressures move in parallel was shown by Weed and Flexner (1921) in dogs, the fluid pressure increase bearing an almost constant relationship of 65% to the venous. Bedford (1935) confirmed this. In looking for the explanation of apparent anomalies in the results of Queckenstedt's test, attention must be focused on the changes attending intracranial venous distension as such, rather than those attending a rising C.S.F. pressure in the ventricles, or elsewhere in the cranial cavity.

Evidence for Posterior-fossa Obstruction by Queckenstedt's Test

After the introduction of ventricular puncture, some workers—e.g., Gardner (1928) and Smyth and Henderson (1938)—sought to show that, on jugular compression, pressure rose higher in the ventricle than in the spinal canal if there was obstruction in the posterior fossa.

O'Connell (1943) drew attention to the fact that rise in pressure, measured through a wide-bore ventricular needle was much more rapid than through a narrow-gauge spinal needle, and that pressure rises in manometers connected to ventricular and spinal needles should not be directly compared.

To eliminate this error, recordings were made of a series of combined ventricular and lumbar punctures, using a blunt fine-bore ventricular needle of the same gauge as the lumbar one. Jugular, thoracic, and abdominal compression were successively performed, and manometer readings were recorded in the ventricle and spinal theca. The series observed included some patients with normal intracranial pressure, and others with proven obstruction at the tentorium and aqueduct, or at the foramen magnum. In none of these did the ventricular pressure rise higher or more rapidly than the lumbar pressure. There was apparently some mechanism whereby pressure was equalised throughout the cerebrospinal axis even when the pathways were obstructed. That this mechanism resides in the vertebral venous system is seen at surgical exposure of the posterior fossa.

Fig. 3—Spinal canal in the injected cadaver filled with dye to C7.

When jugular pressure is applied, there is a rapid outflow of C.S.F. from the fourth ventricle, and the cerebellum is displaced downwards; but, in addition, there is distension of the whole venous bed in the posterior fossa and in the visible upper region of the cervical spinal canal. Plainly, therefore, a rise in pressure caused by distending this venous bed will be transmitted to the C.S.F. pathways whether there is obstruction at the tentorium and fourth ventricle or not. Outflow of C.S.F. from the fourth ventricle may be impeded, but displacement of venous blood into the cerebellar and spinal veins will not. Obstruction in the posterior fossa may sometimes

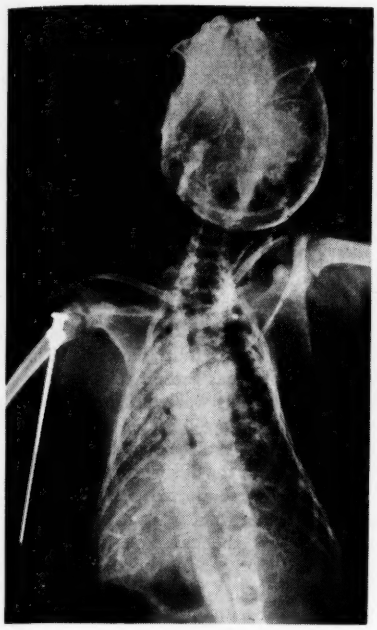

Fig. 4.

Fig. 4—Injection into jugular vein of a rhesus monkey with all jugular veins tied off.

Dye fills the vertebral venous system and escapes to the innominate veins at the lower cervical level.

Fig. 5.

Fig. 5—The monkey's spinal cord, showing the level of venous filling.

delay the rise of fluid in a spinal manometer on jugular compression, but it will not prevent it.

Obstruction in the Cervical Canal

A negative Queckenstedt test in the presence of obstruction in the cervical C.S.F. pathways is less easily understood, but has often been described:

Symonds and Meadows (1937) analysed seven cases of tumour at and below the foramen magnum. In none was a complete manometric block demonstrated, although in four the rise or fall was described as being a little delayed. In the one case in which a satisfactory myelogram was obtained, complete spinal block was demonstrated. These workers were led to conclude that "the degree of subarachnoid block, in relation to the severity of the clinical symptoms, would appear to be less in these cases of high cervical tumour than it is at a lower level". It is more likely that the degree of subarachnoid block is as great, but the methods of detecting it are subject to error.

Martin and Kleyntjens (1950) described three lumbar punctures performed on cases of meningioma at the foramen magnum. Two showed a slow rise and fall of pressure, and one had normal responses to jugular compression. They said "Queckenstedt's test shows little, a complete block being quite exceptional".

Weinstein and Wechsler (1940) described a dermoid tumour in the foramen magnum in which the Queckenstedt responses were normal. Congenital deformities in this region may also cause spinal obstruction. Gustafson and Oldberg (1940) described four lumbar punctures in their series, two partially blocked and two without evidence of block.

List (1941) recorded five cases of platybasia, four partially blocked and one quite free, as judged by spinal manometry. In the last case the spinal cord was reduced by pressure to a fibrous-looking band of small calibre.

I have observed seven cases of neurinoma or meningioma between C1 and C4 in which subarachnoid obstruction appeared to be complete at myelography or operation, although Queckenstedt's test was negative.

Experimental Evidence

It seemed likely that, as in the posterior fossa, the obstruction was being bypassed by transmission of increased venous pressure through the vertebral plexuses. Evidence in favour of this hypothesis was collected from venous-injection studies in man and animals:

A catheter was inserted into the internal jugular vein of patients undergoing carotid angiography. With both jugular veins occluded on the cardiac side of the catheter, injections of contrast material were made. Fig. 1 shows the intracranial venous distension spreading into the internal and external vertebral venous plexuses as low as C6–7. Injections of barium and dye into the jugular veins of cadavers cephalad to the point of venous obstruction confirmed this. X-rays showed a similar filling of the vertebral venous system (fig. 2), and the spinal canal was shown to be filled with dye as far as C7 (fig. 3).

Similar injections were made in monkeys after tying all the jugular veins. X-rays showed the filling of the vertebral veins and the escape back to the innominate veins and the heart (fig. 4). The cord and dura preparation shows that the vertebral venous plexus filling extended, as in the human subjects, to the level of the lower cervical spinal canal (fig. 5).

Provided, therefore, that a cervical spinal tumour does not obstruct the extradural as well as the intradural spinal veins, jugular compression will cause distension of the vertebral venous plexus as low as C6–7, with compression of the theca below the obstruction and a rise in pressure at the lumbar manometer. This rise may not be as great as that normally produced by this distension plus the C.S.F. displaced from within the skull to the spinal canal and thence to the manometer, but it may be sufficient to deceive even an experienced observer. (And in the event,

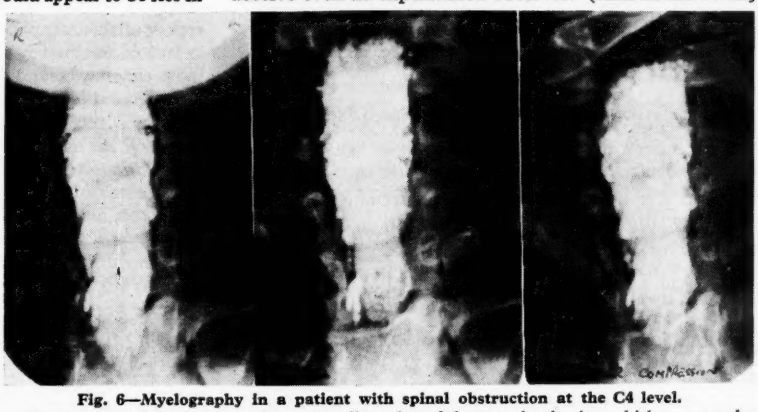

Fig. 6—Myelography in a patient with spinal obstruction at the C4 level.

Compression of the jugular veins causes distension of the extradural veins, which narrows the spinal dural canal and causes the oil column to move cephalad.

most lumbar punctures are delegated to the inexperienced.) This conception is very important for the understanding of C.S.F. mechanics, because many theories about spinal pressures in Queckenstedt's test have been based on the elasticity or otherwise of the dura, which was presumed to be expanded by the increase of C.S.F., volume within. If the theca is compressed from without in the presence of cervical spinal obstruction, it clearly does not matter whether the dura possesses elastic properties or not. If pressure changes are transmitted past a spinal obstruction by extradural venous distension, myelography in such a case should show the oil column narrowing and moving cephalad on jugular compression. Fig. 6 shows that this does in fact occur.

Discussion

The elaborations of Queckenstedt's test by combined puncture methods led to attention being concentrated on changing C.S.F. pressures rather than changing venous pressures. The realisation that C.S.F. and venous pressures move in parallel did not help, because observers came to think in terms of increased ventricular pressure being transmitted via the aqueduct to the cisterna magna and the spinal canal in one continuous wave, with obstruction at any point halting the wave. As a result, it has been suggested at different times that Queckenstedt's test could help in the diagnosis of aqueduct stenosis, acoustic neurinoma, foramen-magnum tumour, or obstruction of a ventriculocisternal (Torkildsen's) tube. The above experiments have shown that it will do none of these things. Nor is it a reliable test for cervical spinal obstruction above the level c5–6, unless the extradural as well as the intradural vertebral veins are completely obstructed by the agent compressing the spinal cord. A negative Queckenstedt's test should not, therefore, be allowed to cloud clinical judgment in patients showing evidence of cervical spinal-cord compression above this level.

Summary

The modifications of Queckenstedt's test are reviewed.

Combined cisternal and spinal puncture methods tended to obscure the importance of venous distension as the primary cause of rising cerebrospinal-fluid pressures, as indicated by manometers.

Clinical and experimental evidence shows that Queckenstedt's test is unreliable in detecting obstruction of the cerebrospinal-fluid pathways above the c6 level.

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ANTICONVULSANTS AS A FACTOR IN MEGALOBLASTIC ANÆMIA IN PREGNANCY

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THERE have been many reports of megaloblastic anæmia induced by anticonvulsant drugs—an association first described by Badenoch in 1954. The relevant literature is well summarised by Hawkins and Meynell (1958). This anæmia has followed the administration of phenobarbitone and phenytoin, and also primidone. In 1956, Girdwood and Lenman drew attention to the similarity in chemical structure between folic acid and these compounds. They suggested that these drugs interfered with folic-acid metabolism. This was confirmed to some extent by Chanarin et al. (1958) who studied a patient in whom megaloblastic anæmia developed after primidone therapy. They found that both the absorption and storage of folic acid in the tissues were normal and concluded that interference with tissue metabolism rather than deficiency of folic acid was the cause of the anæmia. Recently a similar condition was described in a case treated with phenobarbitone (Chanarin et al. 1960). Hawkins and Meynell (1958) investigated the incidence of macrocytic anæmia in large numbers of epileptics who were being maintained with these drugs, and found that this complication was rare. Macrocytosis was common, however, in these patients, and 45% of those receiving phenobarbitone and phenytoin showed this feature. This macrocytosis could be corrected with folic acid.

Megabloblastic anæmia in pregnancy is now being recognised more often, and many reports have been analysed by Chanarin et al. (1959). In the same paper, these workers produced evidence of a folic-acid deficiency in two-thirds of those nearing the end of their pregnancy, and in all patients with twin pregnancy. All pregnant patients with megaloblastic anæmia were found to have a still greater deficiency of folic acid.

Consideration of all these reports suggests that megaloblastic anæmia is more likely to develop when anticonvulsants are used in pregnancy. Possible interference with folic-acid metabolism by these drugs is likely to increase the effect of the relative folic-acid deficiency which may occur in pregnancy. Though Dimsdale (1959) drew attention to the danger of drug-induced megaloblastic anæmia in epileptics during pregnancy, no report of this complication has yet been found.

In a recent survey of 100 cases of megaloblastic anæmia in pregnancy seen at the Rotunda Hospital (Gatenby and Lillie 1960), it was noted that 3 of the cases were epileptics receiving anticonvulsants. The incidence of epilepsy in the general attendance at this hospital is approximately 1 in 400, so that the incidence of 3%

TABLE I—ANTICONVULSANTS AND MEGALOBLASTIC ANÆMIA IN PREGNANCY

Anticonvulsant drugs	Number of patients	Number of pregnancies	Incidence of megaloblastic anæmia
Phenobarbitone	28	48	0
Phenobarbitone and phenytoin	7	7	4*
Phenobarbitone and primidone	1	1	0
Methoin (' Mesontoin ') ..	1	1	0
No treatment	7	13	1
Total	44	70	5

* 1 unconfirmed.

amongst the cases of megaloblastic anæmia suggested a special relationship.

The records of all pregnancies in epileptics over a six-year period (1953 to 1958 inclusive) were studied. 70 pregnancies occurred in 44 epileptics. In 7 of them (13 pregnancies) no anticonvulsants were being administered, because there had been no attacks for many years. A case of megaloblastic anæmia occurred in this group. The remaining cases were divided into groups depending on the anticonvulsants used. Table I shows the relative incidence of megaloblastic anæmia. There were no cases in 48 pregnancies treated with phenobarbitone alone. There were 4 cases (1 unconfirmed by bone-marrow biopsy) out of 7 treated with phenobarbitone combined with phenytoin.

In table II details are shown of the established cases. All had severe megaloblastic anæmia which responded briskly to folic acid by mouth, 20 mg. daily, in spite of continuation of the anticonvulsant treatment. Case C is noteworthy because phenobarbitone alone had been administered in previous pregnancies without the development of megaloblastic anæmia. None of these cases had achlorhydria. Cases A and B are still under observation and neither has shown radiological evidence of gastrointestinal abnormality.

TABLE II—MEGALOBLASTIC ANÆMIA IN PREGNANT EPILEPTICS RECEIVING PHENYTOIN

Case	Pregnancy	1st Hb estimation	Onset of anæmia	Hb at onset	Reticulocyte-peak with folic acid
A	2nd (no treatment during 1st)	11·1 g. per 100 ml. at 24th week	6 weeks antepartum	5·8 g. per 100 ml.	12% on 5th day
B	1st	8·1 g. per 100 ml. at 32nd week	4 weeks antepartum	4·3 g. per 100 ml.	14% on 6th day
C	6th (phenobarbitone during previous pregnancies)	12·4 g. per 100 ml. at 24th week	2 days antepartum	6·4 g. per 100 ml.	15% on 6th day

Summary and Conclusions

From this analysis, it appears that there is a high incidence (3 out of 7) of severe megaloblastic anæmia when phenytoin together with phenobarbitone is used in the treatment of epilepsy in pregnancy. It is recommended that, if phenytoin is being administered to an epileptic during pregnancy, either oral folic-acid supplements should be given during the last trimester, or frequent hæmoglobin estimations should be done to detect the onset of anæmia. If it proves to be megaloblastic, it will respond well to folic acid; the anticonvulsant treatment need not be interrupted.

The incidence of megaloblastic anæmia in 57 pregnancies in epileptics receiving anticonvulsant therapy was studied retrospectively. There were no cases in 48 pregnancies where phenobarbitone alone was used. In 7 pregnancies where phenytoin was used as well as phenobarbitone there were 4 cases (1 unconfirmed) of severe megaloblastic anæmia. Folic acid cured the anæmia in these cases, while allowing the anticonvulsant therapy to be continued.

I wish to thank Dr. E. W. L. Thompson, ex-Master of the Rotunda Hospital, for permission to publish this report of patients who were under his care. I am greatly indebted to Dr. H. C. Moore, pathologist, for his assistance.

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HYPONATRÆMIA AND IMPAIRED RENAL TUBULAR FUNCTION WITH CARCINOMA OF BRONCHUS

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HYPONATRÆMIA is associated with reduced osmotic activity in the extracellular fluid and may occur with lowered, normal, or increased body-sodium stores. It may follow sodium depletion, water retention, or reduction in cellular osmolarity (Schroeder 1949, Sims et al. 1950, Rapoport et al. 1951, Danowski et al. 1955). Renal handling of sodium is variable, and retention or abnormal urinary loss may occur (Rapoport et al. 1951, Schwartz et al. 1957, Orloff et al. 1959).

Hyponatræmia may be found in adrenal failure and severe cardiac, renal, or hepatic disease. It has been described in tuberculosis, cerebral disease, and diabetes, and after excessive loss of body secretions by any route (Danowski et al. 1955, Elkinton 1956).

It may develop during acute lobar pneumonia and tuberculosis (Atchley et al. 1923, Winkler and Crankshaw 1938, Sims et al. 1950). A patient with bronchial carcinoma who showed hyponatræmia and abnormal renal chloride loss was described by Winkler and Crankshaw (1938). Recently, Schwartz et al. (1957) reported two patients with carcinoma of the bronchus in whom hyponatræmia and renal sodium loss probably resulted from inappropriate secretion of antidiuretic hormone. We describe here a further patient with a bronchial neoplasm and hyponatræmia in whom this mechanism did not operate. As well as deficient sodium retention, he had aminoaciduria and increased phosphate excretion. The presence of an acquired renal tubular defect is suggested.

Case-record

A stoker, aged 53, was admitted to the Gordon Hospital on April 17, 1959. For two months he had suffered malaise; non-productive cough, and loss of appetite, with particular revulsion for sweet and starchy food. He had lost 17 lb., and in the previous fortnight had suffered from nausea, with vomiting on four occasions. During the same period he had noted cramps in the abdomen and legs.

He had had a dry mouth and increased thirst for a week before admission. On April 15, he had fainted, and had since been confined to bed. There was no disturbance of micturition, but he had been constipated for a fortnight. He had been a moderate pipe smoker for years, and took little alcohol.

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TABLE I—DAILY INTAKE, OUTPUT, AND SERUM-ELECTROLYTE LEVELS

Day	Sodium intake (mEq.)		Fluid intake (ml.)		Urine (ml. or mEq. daily)				Serum (mEq. per litre or mg. per 100 ml.)					
	Oral	I.V.	Oral	I.V.	Volume	Na	Cl	K	Na	Cl	K	Blood-urea	Total protein	—
1	0	0	1080	0	840	79	48	23	109	82	3·4	35	6·4	..
2	0	0	2160	0	—	—	—	—	111	84	4·5	36	..	..
3	0	0	1920	0	—	—	—	—	—	—	—	—	..	..
4	0	0	1230	0	1380	108	68	57	—	—	—	—	..	Vomit 360 ml.
5	68	0	1860	0	1360	24	46	45	107	78	—	32	..	Vomit 360 ml.
6	102	185	2250	2280	4320	117	177	95	110	77	5·7	35	..	..
7	102	105	2970	3090	2900	128	130	59	121	84	5·6	22	..	..
8	102	185	2010	1980	3360	70	52	12	113	83	4·3	23	..	..
9	102	335	1830	3540	3220	245	280	28	112	80	3·2	24	..	..
10	102	335	1980	3030	1940	168	196	19	123	97	3·9	—	..	..
11	68	300	1590	1650	—	—	—	—	121	95	3·6	21	..	..
12	68	160	750	1140	1140	145	138	34	127	97	4·7	36	..	..
13	68	160	420	1140	1000	122	—	57	126	95	4·3	38	5·4	..
14	68	160	510	1140	970	123	159	75	131	94	4·5	—	..	..
15	68	160	510	1140	1200	156	199	79	132	106	4·7	57	..	..
16	68	160	510	1140	1000	74	90	100	—	—	—	—	..	..
17	68	100	1110	750	815	64	86	88	—	—	—	—	..	..
18	136	0	1350	0	700	55	90	82	133	100	3·2	70	5·1	..
19	136	0	1980	0	—	—	—	—	136	101	5·0	79	..	..
20	0	0	1500	0	790	53	73	79	142	95	4·3	62	5·1	..
21	0	0	1210	0	1040	5	16	125	127	102	4·6	75	..	..

— indicates no measurement; 0 indicates no intake. On days 11 and 19, the collection was lost. Day 1 is a 12-hour collection (6 P.M.–6 A.M.). Day 12 is an 18-hour collection. I.V. = intravenous.

Examination

He was thin and wasted. There was no clinical dehydration or œdema. No abnormal pigmentation was noted. B.P. 100/60 mm. Hg. Respiratory system: fine râles at bases of both lungs, otherwise normal. The tongue was furred, but the mouth was not dry.

Investigations

Daily serum-electrolyte and blood-urea levels; urine-volumes and electrolyte content; and fluid and sodium intakes are shown in table I and in figure.

Blood.—Hæmoglobin 15·0 g. per 100 ml. Erythrocyte-sedimentation rate (Wintrobe) 11 mm. in the first hour. Total white-cell count 9000 per c.mm. (neutrophils 70%, lymphocytes 30%). Liver-function tests, serum-amylase, and serum-cholesterol normal. Serum-albumin 3·9 g. per 100 ml. Serum-globulin 2·5 g. per 100 ml. Random blood-sugar 123 mg. per 100 ml. Wassermann and Kahn tests negative. Serum-alkali reserve (day 13) 24 mEq. per litre. Serum-alkaline phosphatase 7 King-Armstrong units. Serum-calcium 10·6 mg. per 100 ml.; serum-inorganic phosphate 2·2 mg. P per 100 ml. (day 2). Serum-calcium 13·3 mg. per 100 ml.; serum-inorganic phosphate 1·6 mg. P per 100 ml. (day 14). Serum-creatinine 0·6 mg. per 100 ml. (day 14).

Urine.—Urinary calcium 350 mg. per 24 hours. Urinary phosphate 480 mg. P per 24 hours. Urinary creatinine 450 mg. per 24 hours (day 14). Urinary aldosterone excretion (Dr. R. V. Brooks): 1·8 μg. per day (day 16); 1·7 μg. per day (day 17) (normal range 3–8 μg. per day with a mean of 5 μg.). Steroid excretion is shown in table II.

The specific gravity was always within the range 1·010–1·026. No albuminuria. Intermittent glycosuria and ketonuria. There was no glycosuria after day 13, and no ketonuria after day 18. Paper chromatography of urine for aminoacids (Dr. J. H. Wilkinson) showed: (1) a large increase of alanine, glycine, glutamine, histidine, lysine, threonine, and γ-amino butyric acid; (2) a moderate increase of glutamic acid, taurine, and serine; (3) small quantities of valine, leucine, and tyrosine; and (4) traces of methyl histidine and cystine. This pattern of generalised aminoaciduria was present up to the time of death.

Sputum.—No malignant cells.

X-ray of chest.—Mass in left lung near hilum, with bilateral hilar-gland enlargement. Normal pulsation and diaphragmatic movement on fluoroscopy.

Isotope studies (Dr. J. F. Zilva, Dr. J. P. Nicholson).—Total exchangeable sodium (day 12) 2540 mEq. = 54·1 mEq. per kg. (normal range 37–56 mEq. per kg.). Total exchangeable potassium (day 12) 2530 mEq. = 54·1 mEq. per kg. (normal range 37·5–64 mEq. per kg.). Na/K = 1·00 (normal range 0·69–0·95). Bromide-space (day 13) 15·9 litres = 340 ml. per kg.; (day 14) 16·3 litres = 359 ml. per kg. (normal range for his build 248–378 ml. per kg.).

Electrocardiography.—Day 1, alternating atrial flutter and fibrillation. Fast ventricular rate of about 150 beats per minute with both rhythms. Day 5, sinus rhythm, rate 80 beats per minute. Tracings otherwise normal.

Progress

The history of recent cough and the X-ray findings suggested bronchial carcinoma. Severe hyponatræmia (109 mEq. per litre) was found on admission and was associated with abnormal renal sodium loss (79 mEq. in second half of day 1).

He gradually became worse. He was moderately thirsty but too ill to drink unless assisted. During the first four days he took sweetened fruit drinks only, and he continued to refuse food throughout the rest of his illness.

Adrenal failure caused by bilateral metastatic deposits seemed unlikely with a normal blood-urea, a low serum-potassium (3·4 mEq. per litre, day 1), and no pigmentation. His blood-pressure (95–100/60 mm. Hg) was low but this was due to tachycardia, and it rose on day 4 to 120/80, when the arrhythmia reverted to sinus rhythm, though the hyponatræmia persisted (107 mEq. per litre). He was so ill that it seemed best to give extra salt and sodium-retaining hormones until more was known of his adrenal function. On day 5, oral salt in cachets and intravenous saline were begun (table I and figure), and he was encouraged to drink more. He cooperated readily and high intakes were achieved between days 6 and 11. He also took a total of 6 mg. fludrocortisone between days 5 and 9. This potent salt-retainer was used to avoid confusion in estimations of urinary steroid excretion which were done at this time. Fludrocortisone was stopped as soon as these results were known.

With this therapy there was slight improvement, though he remained weak. The serum-sodium rose only slowly, and continued to rise when fludrocortisone was discontinued on day 8 and sodium intake was increased. Intensive sodium therapy was given up to day 11 by which time the serum-sodium level had risen only to 121 mEq. per litre.

Between days 12 and 16, water intake was reduced as much as possible to see if this would affect the renal sodium loss as in the cases of Schwartz et al. (1957). Sodium supplements were continued, so that he also received 1140 ml. fluid daily intravenously, and negative fluid balance was not, therefore, achieved. In this period, with an intake of 228 mEq. sodium daily, the serum-sodium level continued its slow rise to 132 mEq. per litre. From about day 12, his condition steadily worsened, with increasing back pain at the level of the lower part of the thoracic spine, and by day 17 he was very ill. No more intravenous saline was given, but oral supplements were continued for another 2 days. His fluid intake was about

1·5 litres daily. He became emaciated, and bronchopneumonia developed. Finally he lapsed into coma and became clinically dehydrated. There was a terminal rise in blood-urea levels, and the serum-sodium rose to a maximum of 142 mEq. per litre on day 20, though it fell again the following day to 127 mEq. He died on day 22.

Necropsy

At necropsy (Dr. J. S. Cornes) an oat-celled anaplastic carcinoma was discovered, originating in the lingular bronchus, and spreading to the lung, mediastinum, and left supraclavicular lymph-nodes. No other macroscopic spread was found, but histological examination showed infiltration of the liver and spleen by tumour cells.

The kidneys were macroscopically and histologically normal. Histochemical staining (Dr. John Pryse-Davies) showed normal alkaline phosphatase, acid phosphatase, non-specific esterase, succinic dehydrogenase, and lactic dehydrogenase activity. Microdissection (Dr. E. M. Darmady) revealed no abnormality.

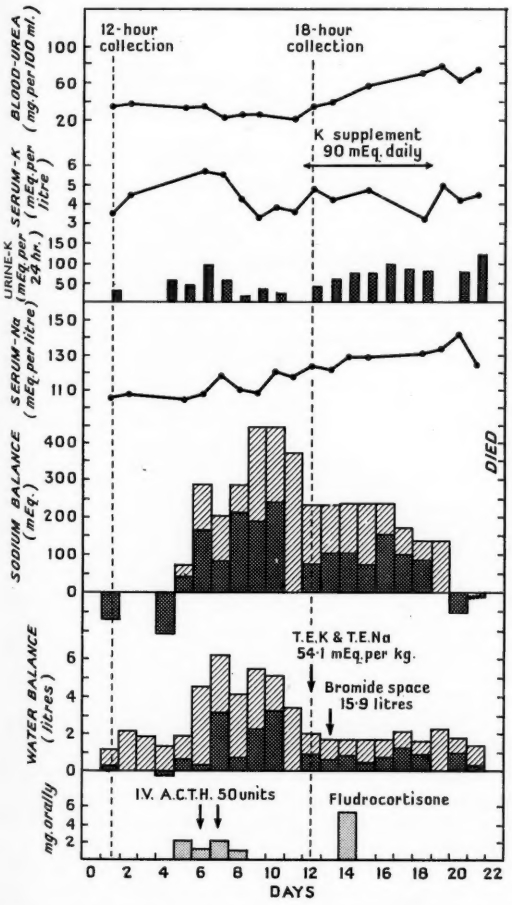
The adrenals were enlarged (combined weight 22 g.) and histologically showed widening of the cortex, principally in the zona fasciculata. Histochemical staining (Dr. Pryse-Davies) for alkaline phosphatase, acid phosphatase, non-specific esterase, succinic dehydrogenase, and steroid 3-β-ol dehydrogenase suggested a hyperactive adrenal gland with increased steroid metabolism.

The parathyroids showed slight uniform enlargement. The pituitary contained a small developmental cyst, 3 mm. in diameter, but otherwise was normal.

TABLE II—URINARY STEROID EXCRETION

Day	Urinary steroids (mg. per 24 hours)		Steroid therapy
	17-hydroxy-steroids	17-keto-steroids	
4	17·8	4·4	Nil
5	7·7	7·0	Fludrocortisone 2 mg. oral
6	66·0	16·8	Fludrocortisone 1 mg. oral Corticotrophin 50 units I.V.*
7	65·0	21·0	Fludrocortisone 2 mg. oral Corticotrophin 50 units I.V.
9	37·0	11·5	Nil
10	2·1	2·0	Nil
20	17·4	7·7	Nil
21	17·7	18·8	Nil

* I.V. = intravenous.



Water and sodium balance calculated from intake and output figures with no allowance for extrarenal loss or water of metabolism.

Daily intake plotted up from baseline. Daily output plotted down from intake figures. Shaded areas above baseline represent positive balance; shaded areas below are negative balance. Intake data only for days, 2, 3, 11, and 19. For potassium, urinary figures only are shown. T.E.K. = total exchangeable potassium. T.E.Na = total exchangeable sodium.

Discussion

The outstanding feature was the extreme hyponatræmia accompanied by malaise, cramps, and thirst. Mechanisms such as decreased cellular osmotic activity or a new steady state, which have been suggested to explain hyponatræmia in severe illness (Sims et al. 1950, Danowski et al. 1955) did not operate in our patient whose hyponatræmia improved as his clinical state deteriorated.

Addison's disease was not present, nor was there any evidence of the usual type of salt-wasting renal disease which is associated with obvious changes in the kidneys (Stanbury and Mahler 1959). The hyponatræmia was clearly associated, however, with deficient renal sodium retention. This is seen on day 1, and on day 4 when 108 mEq. sodium were excreted after at least 4 days without any salt intake. This sodium-leak was partially inhibited by fludrocortisone on day 5, but the presence of more than a trace of urinary sodium at this low serum-level (107 mEq. per litre) suggests that tubular response was impaired. By day 14, a large dose of fludrocortisone had no effect on sodium excretion showing that the tubular defect had increased.

Aldosterone excretion was reduced on days 16 and 17. By then massive sodium repletion had occurred. Extrapolating from the results on day 12 (allowing 10 mEq. daily for extrarenal loss), total exchangeable sodium is estimated at 2866 mEq. for day 16 (approximately 61 mEq. per kg.) and his serum-sodium had risen to a reasonable level for his clinical state. The low aldosterone excretion at this stage is therefore not surprising.

An estimate of the metabolic state on admission may be made from the isotope studies.

On day 13 the bromide-space was 15·9 litres (within normal limits), and before this marked positive water balance had occurred. Allowing 700 ml. daily as the balance between insensible loss and water of metabolism, a positive balance of 6·2 litres occurred between days 7 and 11. Unfortunately, the urine on day 11 was lost, but the intake makes a negative balance unlikely. Ignoring this day, a positive balance of approximately 5·6 litres existed between days 5 and 13. Thus, on day 6, the extracellular fluid volume was estimated at 10·3 litres (about 220 ml. per kg.). This figure would have changed little from the time of his admission, and is abnormally low.

Total exchangeable sodium on day 12 was 2540 mEq. Ignoring day 11 again, cumulative sodium retention from day 5 to day 12 was 972 mEq. The amount of food taken was

negligible, and allowing 10 mEq. per day for extrarenal sodium loss, the estimate for total exchangeable sodium on day 5 was, at most, 1640 mEq. (approximately 35 mEq. per kg.)—an abnormally low figure. Total exchangeable potassium on day 12 was 2540 mEq., and cumulative potassium loss in the previous week was 258 mEq. (again ignoring day 11). Allowing 10 mEq. daily for unmeasured potassium loss, the total exchangeable potassium on day 5 was estimated at about 2868 mEq. (approximately 61 mEq. per kg.), which is in the upper normal range.

Thus it appears that our patient on admission was depleted of sodium with a reduced extracellular-fluid space.

In their two patients, Schwartz et al. (1957) thought that carcinoma in some way caused inappropriate secretion of antidiuretic hormone. This produced sodium loss by increased glomerular filtration and, because extracellular volume did not fall, by a failure of aldosterone secretion to rise with sodium depletion. Both patients had severe hyponatræmia, in one case as low as 103 mEq. per litre, with few symptoms. In one the extracellular volume was measured, and was found to be raised.

In our patient, the low estimate for extracellular space on admission makes it unlikely that inappropriate secretion of antidiuretic hormone caused his sodium loss. The increased thirst in the week preceding admission is in keeping with this view, though thirst can occur with an increase in body water (Wynn and Rob 1954).

The effect of water restriction (days 12–16) was unimpressive. There was no dramatic reduction in urinary sodium loss as in the patients of Schwartz et al. (1957) and though restriction of water was not severe, it was more than was needed in one of their cases to reverse sodium loss. Administration of large amounts of fluid caused improvement, rather than deterioration, and sodium given in this phase was largely retained in contrast to the results in their patients. The poor response to salt-retaining hormones is a further point of distinction, and in addition our patient probably produced hypotonic urine on some days (e.g., day 8, table 1) when specific gravity was not recorded, whereas in the cases of Schwartz et al. (1957) urine was hypertonic to plasma.

In our patient, it seems that the renal sodium leak was due to impaired tubular function. With liberal intakes, sodium loss was not excessive, and repletion was easily achieved. However, when sodium intake was low, an obligatory renal salt-loss was revealed, leading to sodium depletion and, eventually, hyponatræmia.

This defective reabsorption of sodium, together with intermittent ketonuria and glycosuria, suggested proximal tubular damage, and investigation led to the unusual finding of generalised aminoaciduria. Other recognised causes of renal aminoaciduria were absent, and there was no evidence of the adult Fanconi syndrome (Wallis and Engle 1957) in which sodium loss, in particular, does not occur. Overflow aminoaciduria may be found with increased protein breakdown, and since the plasma-aminoacid level was not estimated, this is a possibility in our patient, though other features favour its renal origin.

Impaired phosphate reabsorption and low serum-phosphate levels accompanied the aminoaciduria, providing further evidence of proximal tubular damage. The terminal hypercalcæmia and necropsy findings of parathyroid gland enlargement were probably due to secondary hyperparathyroidism.

The distal tubular exchange mechanism of potassium for sodium could function normally as shown by falling sodium excretion in the last week, with increased potassium excretion and K/Na ratios, particularly evident on day 21. 24-hour creatinine-clearance on day 14 was reduced, and rising blood-urea levels were recorded in the last week, indicating progressive reduction in glomerular filtration. This might have reduced the load on the proximal tubules to a level at which they could function competently. The resultant fall in distal tubular flow might then allow the efficient cation exchange and sodium conservation seen on day 21. A diminution in proximal tubular load would also explain the disappearance of glycosuria and ketonuria in the week before death.

A defect in proximal tubular function was therefore thought to be present, and a similar defect was postulated by Rapoport et al. (1957) as the cause of hyponatræmia in their patients with tuberculous meningitis. However it remains difficult to explain the urinary composition on days 1 and 4. The metabolic state on admission should have resulted in maximal aldosterone secretion. The modest potassium excretion and low urinary K/Na ratio at this time is surprising and, with the poor response to administered steroids, suggests that distal tubular function was also impaired.

Summary

Severe hyponatræmia developed in a man of 53 with bronchial carcinoma. He showed poor renal sodium conservation which, with negligible intake because of anorexia, had caused sodium depletion.

Repletion was easily achieved and fluid restriction did not affect the sodium loss. Metabolic studies suggested that, on admission, he was depleted of sodium, with a reduced extracellular-fluid volume.

There was no evidence of adrenal failure, and at necropsy the adrenal glands were enlarged and showed signs of hyperactivity.

The renal response to fludrocortisone and corticotrophin was poor. There was no clinical evidence of any of the usual types of salt-wasting renal disease, and at necropsy the kidneys were normal on detailed histological examination.

There was evidence of functional damage to the proximal tubules with generalised aminoaciduria, glycosuria, ketonuria, and increased phosphate excretion. Aminoaciduria was constant throughout, but glycosuria and ketonuria were intermittent and disappeared in the last week.

The distal tubular exchange of sodium for potassium was active terminally, though perhaps not on admission. It is suggested that the sodium loss was mainly due to proximal tubular damage, and that the bronchial carcinoma had caused this unusual derangement of tubular function.

We wish to thank Dr. R. D. Tonkin, under whose care this patient was admitted, for permission to report this case, and Dr. R. I. S. Bayliss for advice on the manuscript. The microdissection of the kidneys was carried out by Dr. E. M. Darmady. The urinary amino-acid determinations were performed by Dr. J. H. Wilkinson. We are indebted to Dr. R. V. Brooks for the urinary aldosterone assays. Details of the adrenal and renal histochemical studies were kindly provided by Dr. John Pryse-Davies. The results of the isotope studies were provided by Dr. J. F. Zilva and Dr. J. P. Nicholson. The necropsy was performed by Dr. J. S. Cornes. The figure was prepared by the department of medical illustration, Guy's Hospital.

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POSTPARTUM PRE-ECLAMPSIA

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A WOMAN, aged 19, had an eclamptic fit fifteen hours after she had her first baby. She had given no evidence of pre-eclamptic toxæmia while pregnant, or during her eight-hour labour. An episiotomy was necessary for delivery, and, in the course of its repair, she seemed drowsier than would have been expected from the 100 mg. pethidine and the gas-and-air analgesi she had received during labour. That night she slept uneasily, complaining of epigastric discomfort, and at 6 A.M. next day her blood-pressure (B.P.) was 140/90 mm. Hg: an hour later she had the fit.

The patient was first seen during the sixteenth week of pregnancy. No history of serious illness, previous pregnancy, or fits was given (this was confirmed in the puerperium). Her general condition was excellent. Hæmoglobin 87% (Haldane); blood-group B, rhesus-positive; Kahn-negative. The B.P. was 130/70, weight 105 lb., and her urine showed no abnormality. Thirteen visits were made during the pregnancy. Apart from a trace of albumin in a morning specimen of urine at the thirty-seventh week, and slight swelling of the ankles the week before that, the only abnormality of the pregnancy was a degree of hydramnios at the thirtieth week sufficient to warrant an X-ray of the abdomen. The hydramnios decreased slowly but was still present at term. The weight rose gradually to 128 lb. at term, and fell 1 lb. in the following week. The blood-pressure remained between 110/60 and 120/80 during the pregnancy.

Progress

Day 1.—A healthy 6½ lb. infant, born ten days after the estimated delivery date. The labour was uneventful. Total blood loss 8 oz.; 0·5 mg. of ergometrine was given intramuscularly after delivery of the placenta.

Day 2.—B.P. after the fit, 140/90. There was no residual paralysis, but facial œdema was noted and this increased during the next few hours. The patient was sedated with barbiturates, and given a low-salt diet. During the day her B.P. remained at about 130/90. Morphine was given that night as she complained of headache.

Day 3.—The B.P. fell until it was 125/80 in the evening; the œdema subsided; and the patient had no complaints.

Day 4.—About seventy-two hours after delivery the frontal headache and facial œdema returned. The breasts became engorged and treatment for the suppression of lactation was begun. Her temperature rose until it was 102·6°F by the evening. She was moved into an air-conditioned room, and sedated with 6 g. amylobarbitone six-hourly and 25 mg. chlorpromazine orally twice daily. The hæmoglobin was 88% (Haldane) and the hæmotocrit value 40%.

Day 5.—A morning catheter specimen of urine contained 200 mg. albumin per 100 ml., 15–25 red blood corpuscles, and 3–4 white corpuscles per high power-field; it was sterile. A Foley catheter was introduced, and nitrofurantoin 100 mg. given six-hourly to prevent a urinary infection. She passed 1290 ml. of urine that day. The œdema and headaches remained. The temperature fell to 98·4° by the evening. The blood-pressure, however, started to rise during the day.

Day 6.—The B.P. continued to rise until in the evening it reached 170/100. At that point 12·5 mg. hydrallazine was given orally: this was followed an hour later by a fall in B.P. to 145/100. The dose was increased by stages to 37·5 mg. four-hourly. The B.P. fell gradually, until on the tenth day it was consistently 130/80 at the time that the next dose was due.

The typical pre-eclamptic facies and headache remained until the sixth day when, along with the albuminuria, they started to subside. On the ninth day the catheter was withdrawn, the administration of chlorpromazine was stopped, and the patient was moved out of the air-conditioned room. The output of urine did not fall below 950 ml. per twenty-four hours, nor did the blood-urea rise above 20 mg. per 100 ml. and the blood-electrolytes remained within normal limits.

The hydrallazine was continued until the fifteenth puerperal day. It was gradually reduced thereafter, and was stopped on the twentieth day. The B.P. had then been 105/75 for three days; there was an occasional trace of albuminuria; and the patient had no symptoms. The baby was bottle-fed and thriving.

Six weeks after delivery the patient was seen at the postnatal clinic. She had suffered no headaches or swelling of the ankles since leaving the hospital, nor were there any other complaints. The urine contained no albumin, the B.P. was 110/75, and she weighed 106 lb. Uterine involution was satisfactory.

Discussion

Stander et al. (1946) described 21 cases of eclampsia occurring within thirty hours of delivery: 13 of these had shown no evidence of antepartum pre-eclamptic toxæmia. In 9 cases of postpartum convulsions in the first twenty-four hours of the puerperium published by Hofmeister and Brown (1953), 2 had given no previous signs of pre-eclampsia. Theobald (1955) quotes 4 cases of antenatal eclampsia in patients known to have been normal at some time in the twenty-four hours before the fits. It is clear that this fulminating eclampsia can also occur in the puerperium. It is not, however, common for a patient to develop the pre-eclamptic syndrome for the first time after delivery and after a fit; in none of these series is it mentioned. Hamilton (1953) states that hypertension and convulsions may be produced by intravenous ergometrine given at the time of delivery, but this is not accompanied by œdema and albuminuria, and the blood-pressure usually settles within four hours.

There is a school of thought which holds that pre-eclamptic toxæmia and eclampsia are due to increased myometrial tension, pointing out that twins and hydatidiform moles are examples of an overdistended uterus being frequently associated with pre-eclampsia. Theobald (1955) gives as one of his essential criteria for any hypothesis purporting to explain the genesis of eclampsia that it must afford a reasonable explanation of eclampsia occurring up to four days after delivery of the placenta, and many find this a stumbling-block in accepting this hypothesis.

A possible explanation of my case can be obtained from the concept of pregnancy as "a kind of physiological Cushing's syndrome" propounded by J. S. L. Browne and elaborated by F. J. Browne (1958). In this it is held that the adrenal cortex undergoes hyperplasia in pregnancy under the influence of the large quantities of corticotrophin produced by the hypertrophied anterior pituitary and the placenta, and Poideven's (1959) demonstration of the relationship of striæ gravidarum to adrenal cortical hyperfunction supports it. The excess of corticosteroids produced has been demonstrated by Gemzell (1953) who

DR. REES & OTHERS: REFERENCES

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found that in the last three months of normal pregnancy the blood-level of 17-hydroxycorticosteroids is four times the normal non-pregnant value. This would produce œdema and hypertension were it not that the healthy placenta inactivates the excess of pressor substance. If, however, placental function is diminished below some critical value by placental ischæmia (as may occur in essential hypertension, in a primigravid uterus which has hypoplastic vessels, or in twin pregnancy) pre-eclampsia develops. The same investigator has also shown that immediately after delivery the corticosteroid level is seven times the normal, but that it falls to the non-pregnant level by the sixth puerperal day. It might be expected that this would produce hypertension as the placenta is no longer present. This, in fact, happens. Browne (1958) quotes findings, in Sydney and London, that 20–30% of women whose blood-pressure remains within normal limits throughout pregnancy and labour are hypertensive in the first three days after delivery.

I have recently seen two patients in whom the pre-eclamptic syndrome developed after normal pregnancies; a third patient developed hypertension after a forceps delivery, during which she received two doses of 0·5 mg. ergometrine each.

Case 1.—A patient, whose first pregnancy and puerperium were quite uneventful, delivered her second child after a three-and-a-half-hour labour at term, and was given 0·5 mg. ergometrine intramuscularly. Antenatally her B.P. had not risen above 125/75, nor was there any other abnormality. One and a half hours after delivery she vomited and complained of headache. Her B.P. was then 180/110. She was sedated with morphine. Six hours later the headache was still present and she had developed generalised œdema with typical pre-eclamptic facies. The B.P. was 155/100, and a swab specimen of urine contained albumin ++. Sedation was continued and the œdema gradually settled. Thirty-six hours after delivery the headache and œdema had disappeared, the B.P. was 125/85, but there was still albuminuria. Thereafter the puerperium continued normally. The patient was discharged on the tenth puerperal day, her B.P. being 130/80, and the urine contained a trace of albumin.

Case 2.—Normal labour after a second uneventful pregnancy. A single intramuscular dose of ergometrine was given after delivery. On the third day of the puerperium the patient developed headache, hypertension (132/100) and gross generalised œdema. These increased in severity on the fourth day and then responded to rest in bed, sedation, and chlorothiazide therapy. She left hospital on the twelfth day, but the œdema recurred when she was at home and did not disappear for some weeks. The patient was a midwife, and remembered a similar sequence of events after her first confinement.

Case 3.—A primigravida with an uneventful antenatal course, the highest B.P. reading being 120/65. After a twenty-five-hour labour she was delivered with forceps under pudendal block anæsthesia, because of second-stage delay. Ergometrine 0·5 mg. was given with delivery of the anterior shoulder. As the uterus tended to relax an intramuscular dose of 0·5 mg. ergometrine was given. One hour and fifty minutes after delivery she complained of nausea; the B.P. was then 170/105. The patient was sedated with amylobarbitone. The B.P. fell steadily: four hours after delivery it was 125/80, and it did not rise again. There was no œdema.

The development of the pre-eclamptic syndrome after emptying of the uterus in the first two of these cases could easily be interpreted in terms of the foregoing hypothesis. A similar transient hypertension to that occurring in the third case was noted after a cæsarean section where the patient also had a double dose of ergometrine, and it is probable that the rise in blood-pressure was caused by the ergometrine in both cases.

Summary

A case of postpartum pre-eclampsia with one eclamptic fit is described in a patient who had hydramnios but no pre-eclamptic toxæmia before delivery.

A possible explanation is that the already high blood-levels of 17-hydroxycorticosteroids during the last three months of pregnancy rise still more immediately after delivery, and do not fall to normal until the sixth puerperal day. Pre-eclampsia will occur in this period if, through ischæmia, placental function is reduced below some critical value. Postpartum pre-eclampsia may arise once the placenta is delivered, because the excess of pressor substance is then no longer inactivated, and hypertension and œdema result.

I wish to thank Dr. J. H. Hewitt for his encouragement in the preparation of this paper, and the Director-General of Medical Services, Royal Air Force, for permission to publish.

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Preliminary Communication

HYALINE MEMBRANE FOLLOWING TOTAL BODY RADIATION

RELATION TO LUNG PLASMINOGEN ACTIVATOR

IN 1940 Warren and Spencer [1] pointed out that hyaline-membrane formation was the most definite of all changes produced in the lung by X-irradiation of the chest. These changes were observed after " chest wall doses " of 800–15,000r. Though hyaline membrane was by no means pathognomonic of irradiation lung damage, its association with œdema, fibrosis, diminished inflammatory response, and hyalinisation of arterial walls was sufficiently unusual to enable irradiated lung to be distinguished from the non-irradiated. The pathogenesis of this lesion is not understood.[2]

Recently patients with far-advanced malignancies have been subjected to total body radiation (T.B.R.) at the National Naval Medical Center, utilising a $4\pi^{60}$Co irradiator.[3] Clinical results are to be described elsewhere, but we wish to report that at necropsy hyaline membrane and fibrinoid deposits have been prominent in cases surviving at least two weeks after treatment.

Lieberman [4] has recently associated hyaline-membrane disease of children with deficiency of plasminogen activator in the lung. This tissue enzyme converts plasminogen to plasmin, the active fibrinolytic enzyme of the body. Lung normally contains high levels of plasminogen activator.[4 5] Lieberman reasons that because of the relative insolubility of lung plasminogen activator [5] its action is primarily local. In situations where there may be a pathological deposition of fibrin in the lung, it would

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LUNG ACTIVATOR ASSAY

Dose T.B.R.	Number of dogs	Day after radiation	Result
1000r	1	3	Positive
	1	6	Negative*
	1	7	Negative*
800r	1	4 hrs.	Positive
	1	8	Negative
	1	9	Negative
	1	10	Negative*
	1	11	Negative
	1	12	Negative
700r	1	9	Positive
600r	1	9	Positive
Controls	10	..	Positive

* Assayed for inhibitor—all positive.

be the activator's function to activate the fibrinolytic system and effect the fibrin's removal. Persistence of fibrin deposits due to a defect in this system would lead to hyaline-membrane formation [4] and fibrosis.

The fibrin-plate technique of Astrup as outlined by Lieberman [4] was utilised and in addition fortified with 0·01 *M* Ca ions. The latter are added to saturate the citrate of commercial bovine fibrinogen and obviate non-enzymatic lysis of the fibrin.[6] This technique is considered quite sensitive and specific for the detection of plasminogen activators.[7]

OBSERVATIONS

Lieberman [4] has well documented the presence of activator in normal adult lung and this has been confirmed by us in a case of traumatic death. Two men who had undergone T.B.R. therapy were investigated. One had received 450r T.B.R. for disseminated lung cancer 18 days before death, and the other 1500r T.B.R. 15 days before death. The latter had no associated malignancy and had been treated in conjunction with an attempted transplant of kidney. In both instances hyaline membrane was present in the lung. Intensity of membrane formation has generally been associated with high dosage and survival for more than 6–8 weeks after therapy.[2] In both cases the assay of lung tissue failed to demonstrate any plasminogen activator.

To follow the sequence of events eleven dogs were subjected to T.B.R. in similar fashion to the human subjects. The table shows the results of assays of lung activator at various intervals in these eleven dogs and in ten controls.

The absence of activator in the irradiated animals could be due to inhibition. Portions of lungs from three animals with absence of activator were homogenised and the homogenate was mixed with equal volumes of an active lung homogenate. In each case the activity of the normal lung was completely inhibited. The animals tested are indicated in the table by an asterisk.

None of the lung sections showed the classical signs of radiation lung damage, and often they were described as normal. Since several weeks are generally required for the development of hyaline membrane,[2] and the animals in this dose range of T.B.R. seldom survive beyond the second week, this finding might be expected.

COMMENT

In two men treated by total body radiation, hyaline membrane was found in the lung. Plasminogen activator was apparently absent.

The enzyme soon disappeared from the lungs of dogs given T.B.R. of 800–1000r, but these showed no morphologic change suggestive of the first stage of either hyaline membrane or fibrosis.

Our findings are consistent with the production, in irradiated lung, of a potent inhibitor of plasminogen activation.

Further studies are in progress to assess the influence of drugs and radiation technique on the activator system in the lung.

The opinions expressed in this paper are those of the authors and not necessarily those of the Navy Department.

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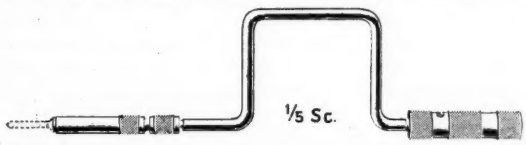
New Inventions

A BRACE SCREWDRIVER

ALTHOUGH Fitzgerald described a brace screwdriver several years ago,[1] this has never become popular, and the ease with which screws can be inserted by its use has not been generally appreciated.

Repeated gripping of a conventional screwdriver, and pronating and supinating the forearm, can be very tiring—as many as 150 repetitions of this movement being necessary to insert four screws. The brace screwdriver, by its continuous action, removes this strain and also eliminates the inertia of the screw which develops each time it stops turning. The



lessened resistance diminishes the chance of the screw breaking, and the brace gives better control.

The type of brace is important. The model here illustrated, adapted from a socket spanner, can be held firmly along the axis of the screw. There should be no sleeve on the crank handle so that the hand can appreciate small changes in resistance during insertion. Some screw-holding attachment is essential. A simple holding sleeve, made by the London Splint Co. for one of their conventional screwdrivers, was used at first and proved quite satisfactory. The Williams screw-holding device, made by Chas. F. Thackray, Ltd., although more elaborate, could also be used for this purpose. The brace here illustrated uses the Stryker screw-holding attachment. The Stryker attachment was devised for a power-driven continuously rotating screwdriver, and it is particularly suited to the rotary action of the brace. It has the great advantage over any other screw-holding attachments that the chuck not only releases the screw head automatically but also allows the screw to be fully driven home and tightened by one continuous action, thereby avoiding the need to complete the last few turns with a conventional screwdriver.

This final pattern of brace screwdriver is available from Messrs. Down Bros., Ltd., 21, St. Thomas' Street, London, S.E.1. By its use screws can be inserted into the upper femur with appreciably greater speed and precision than by any previously available hand-driven device.

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Reviews of Books

The Problem of Acute Hypothermia

Editor: P. M. STARKOV. Translated from the Russian by R. E. HAMMOND. Editor of English edition: E. NEIL, M.D., professor of physiology, Middlesex Hospital Medical School. London: Pergamon Press. 1960. Pp. 329. 70*s*.

THIS book contains the results of many years research in Professor Starkov's department in Omsk. There are twenty-eight articles by the fourteen workers concerned; and they are all physiological, though the hope is expressed that some of the conclusions may be put to practical use. The subject titles alone make interesting reading, for, as might be expected, they imply a quite different approach to the physiology of hypothermia from that in the Western world, where much of the work has been planned pragmatically, according to the needs and problems of the operating-theatre, and not so much concern, perhaps, is felt about the basic differences between the body functions at normal temperature and those revealed during hypothermia. Physiologists will therefore welcome the results of study on such fundamentals as cold effects on blood-flow in limbs and viscera, on the effects of direct cerebral cooling, and the use in hypothermia investigation of the values accorded by such familiar parameters as those of the heart-lung preparation, decerebrate cat, isolated rat uterus, and skeletal muscle. Behaviour and conditioned reflexes in puppies and adult dogs are subjects of natural interest to Russian physiologists, and the response of these nervous patterns to hypothermia is the subject of one of Professor Starkov's own articles.

The publishers regret that for speed and economy of production the text is in typescript photolithography, but the quality of the pages is even and good, and the content more than makes up for any deficiency. The translation is commendably clear.

Lectures on Hæmatology

Editor: F. J. G. HAYHOE, M.D., M.R.C.P., department of medicine, University of Cambridge. London: Cambridge University Press. 1960. Pp. 247. 60*s*.

THESE lectures were delivered at Cambridge in December, 1959, at a course for physicians and clinical pathologists "having hæmatology as one of their main interests". Four of these lectures will interest any hæmatologist: J. V. Dacie gives some facts from his unique experience in hæmolytic anæmia; W. M. Davidson provides an excellent account of iron metabolism and treatment; G. Wetherley-Mein describes interestingly and practically what is meant by "myeloproliferative syndromes"; and R. M. Hardisty makes a gallant attempt to bring together in a moderately coherent account what we now know about hæmostatic processes. The other lectures are good, sometimes very good, reporting work that will be familiar to many hæmatologists. R. H. Girdwood on megaloblastic anæmias, George Discombe on transfusion hazards, and J. C. White on hæmoglobin variants summarise their already published work. Dr. Hayhoe himself draws on some pages from his recent book on leukæmia. Richard Doll writes on the incidence of leukæmia and the significance of environmental factors, D. A. G. Galton on the chemotherapy of leukæmia, G. I. C. Ingram on congenital and acquired disorders of blood coagulation, and J. F. Ackroyd on the pathogenesis of purpura. H. E. M. Kay brings together a useful summary of published results on attempts to use marrow transplants in the treatment of leukæmia.

This sort of book falls between two stools: the specialist in hæmatology will be interested only in the first four lectures we mentioned; the more general physician or pathologist with a main interest in hæmatology will hardly wish to buy a set of lectures that will need revision in a short time, especially when he can buy a whole textbook of hæmatology, containing nearly everything in this volume and a lot more, for rather less. This volume is to be one of a series: why not publish the others in a less expensive form—say, paper back with plastic binding and without some of the illustrations, none of which, in this hæmatology volume, are really necessary?

Chemical Micromethods in Clinical Medicine

R. H. WILKINSON, M.D., assistant chemical pathologist, The Hospital for Sick Children, London. Oxford: Blackwell Scientific Publications. 1960. Pp. 121. 40*s*.

EMPHASIS on micromethods in chemical pathology has increased steadily during the past twenty years. It was gradually realised that blood-sugar and blood-urea were not the only substances that could be measured using capillary blood and that it was obviously more considerate and convenient to take small samples of capillary blood by needle-prick than larger ones from a vein by syringe. It has also become clear that small amounts of heparinised blood may yield as much plasma as larger amounts of clotted blood can yield serum. These considerations apply particularly to pædiatrics, and in this country notable contributions to microchemical methods have come from The Hospital for Sick Children, Great Ormond Street, and some very important ones from the author of this little book. There are only about 100 pages of text, of which 10 are taken up by illustrations, not all of them essential (a page is used for a photograph of a Van Slyke manometer and another for its micro version; and almost a whole page is given to a photograph of the EEL flame photometer, which has been in routine use in virtually all pathology laboratories for many years). Most of the methods for examining blood in a pædiatric hospital are clearly described (the estimation of serum-iron is not among them). Micromethods only are considered, and this excludes many important pædiatric investigations of urine and fæces.

Principles of Animal Virology (2nd ed. New York and London: Academic Press. 1960. Pp. 490. 86*s*.).—This book, edited by Sir Macfarlane Burnet, O.M., F.R.S., is very different from Burnet and Stanley's *The Viruses*,[1] and is much more concerned with viruses of men and animals as agents of disease. A particularly interesting aspect is its emphasis on the ecology of viruses and on evolutionary aspects of virus development. Much of the book is written from a very personal viewpoint, and the references are selective rather than comprehensive. Nearly half the text of the first edition, which appeared five years ago, has been rewritten.

Preventive Medicine and Public Health (4th ed. London: H. K. Lewis. 1960. Pp. 316. 27*s*. 6*d*.).—It is no easy matter in these days to write a universally acceptable student textbook on public health; there is still so much diversity of opinion about the legitimate scope of the subject and so much variation from school to school in attention given to it. Prof. Fred Grundy's book aims to be an introduction for students and practitioners and it obviously meets a want, for it is now in its fourth edition in ten years. The book is necessarily simple in its approach, and some of its pictures could perhaps be shed without much loss; but it does provide an outline of basic principles and for the zealous it offers suggestions for further reading.

Hypnoanalysis (New York: Grove Press. London: John Calder. 1960. Pp. 342. 16*s*. 6*d*.).—Dr. Lewis R. Wolberg's wide experience of hypnosis is well known, and some of his writings have become classics. This paperback, which is a reprint of a 1945 Grune & Stratton edition, is devoted to the use of hypnotic techniques during psychoanalysis, in this case Freudian. The first 136 pages describe the treatment of one patient, then follows a 21-page "dynamic formulation" by Dr. A. Kardiner, and in the final 179 pages Dr. Wolberg suggests the various ways in which hypnosis can be of use in psychoanalytic treatment. The case-report is certainly of great interest, notwithstanding the doubt in diagnosis, and Dr. Wolberg writes better than most analysts; but the work will do little to convince the sceptical. Practitioners who use either of these techniques will find the book interesting, but there must be serious reservations about presenting this new edition to the large lay readership for which it is presumably intended.

1. See *Lancet*, 1959, ii, 548; *ibid*. Oct. 29, 1960, p. 961.

THE LANCET

LONDON 5 NOVEMBER 1960

Coming Home and Going Abroad

ON achieving independence, a Colony naturally wants to have all its services manned by its own people; and that is something to which every new nation should look forward. But commonly the wellbeing and progress of Colonies have depended largely on the devoted work of administrative and professional officers from overseas; and usually these ought to go on with that work until there are enough properly qualified indigenous officers to replace them. Unfortunately the insecurity of a new regime may lead to an exodus of many of the men and women whom the new country will most need in the next few years. The anxieties of a Civil Servant in a country likely to become self-governing are well depicted in the white-paper [1] issued last week:

". . . the sense of vocation which led him into the Public Service in an overseas territory still remains, but he is beset by uncertainty as to the extent to which he will be able to fulfil it under the new conditions: his status in public affairs is changing and very often he and perhaps his family also are subject to discomforts stemming naturally from a period of rapid political change; and until reassurance is given him on the shape of his future he must live through a period of extreme doubt about the years ahead."

To prevent the " tragic waste of human skills and wisdom " inevitable where a service runs down through departure of its key members, the British Government, as announced last July,[2] are offering ten-year agreements to most Colonial territories by which the territory need pay little more to employ someone from overseas than to employ one of its own nationals.[3] In respect of some 21,000 officers of the Overseas Civil Service (appointed by the Colonial Office or the Crown Agents) the Government will be responsible (1) for the expatriation or inducement element often added to basic salaries to attract overseas candidates, (2) for the corresponding part of the pension, (3) for education and children's allowances, (4) for half the cost of leave passages, and (5) for half the cost of compensation payable for premature retirement. While this excellent scheme can be looked on as an act of justice towards people who have been encouraged to take overseas appointments under the Crown, it is also much more. It is an important offer of assistance, during the transition period, to territories which may see the advantages of retaining expatriate officers but might otherwise be unable to keep them. The cost to Britain is estimated at between £12 million and £16 million a year.

Two years ago at the British Medical Association's conference on overseas appointments,[4] one speaker said bluntly that if men are expected to go and work in the Colonial Service, arrangements must be made for them when they come back. An attractive suggestion which is firmly turned down in an appendix to the white-paper is that the Civil Services at home and abroad should be unified, so that members could expect a full career, if not in the Colonies then at home. But in point of fact the home Civil Service, with an administrative staff of less than 2500, can offer comparatively few openings to men returning from abroad; and the vacancies now likely to be offered to such men by other Colonies will usually be in a basic grade, and for only one or two tours of service. The creation of a unified service based on the United Kingdom would, it is felt, give a false impression, because it could create no jobs for which members of the Overseas Civil Service are not already eligible. Though some of these will enter the home Civil Service, or the Foreign Service, or may be assigned to other countries under technical-assistance agreements or similar arrangements, they cannot be sure of such employment; and for this reason the Colonial Office in July, 1957, set up an Overseas Services Resettlement Bureau to find them, if need be, alternative posts. Of 1710 applicants the bureau has so far found employment for over 1000—about 500 of them in the past year. The Government hope that " the knowledge that the Bureau will be there to assist them when required will both encourage officers to continue their overseas service, and new recruits to join it ".

To the returning doctor even less than to the administrator can the Government guarantee a post at home; and latterly the difficulty of getting one has been a misfortune both to those who applied and to the public which has often been denied their services. The Government's own medical establishment is small and specialised; and the Ministry of Health, even when it accepts a moral obligation to get a particular specialist appointed or reappointed to the National Health Service, finds regional hospital boards properly reluctant to choose anyone other than the best applicant for the job. If the specialist has difficulty in establishing himself in this country, the difficulty can be even greater for general-duty officers who, though they may have been doing general practice at a high level, have usually been unable to secure National Health Service practices against the competition of younger men who have stayed here. The gloom over our failure to reabsorb so many of our able people who have had the courage and enterprise to work abroad was epitomised in the statement of a speaker, two years ago, that he could not see how general-duty medical officers returning from Colonial service can fit in anywhere at any level in our medical services. And this gloom seems as inspissated as ever, causing even the most sanguine to speak of this problem of medical resettlement as largely insoluble. But are we not in fact dealing with a hangover rather than an incurable illness? If, as LAFITTE and SQUIRE [5] say, this country is shortly going to wake up and find

1. Service with Overseas Governments. Cmnd. 1193. H.M. Stationery Office. Pp. 22. 1s. 3d.
2. *Hansard*, July 28, 1960, col. 1869.
3. The offer will also be made to Nigeria (now independent), to Sierra Leone (to be independent next April), to Singapore, and to Northern Rhodesia and Nyasaland. The Bahamas, Bermuda, Brunei, and Hong Kong are excluded from the scheme.
4. See *Lancet*, 1958, ii, 1111.
5. Lafitte, F., Squire, J. R. *ibid.* Sept. 3, 1960, p. 538.

itself extremely short of doctors, those who might be willing to reduce the shortage can take new heart.

Similarly the apparent risks of going abroad for a few years, on secondment or otherwise, may begin to bulk less large in the minds of candidates. The Government are in favour of secondment from their own services here, and propose to have talks with representative bodies of employers " to seek their agreement to releasing staff on loan "—paying " in appropriate cases . . . the differential between the terms of the overseas appointment and the local salary ". If there are still senior members of the profession who are inclined to discourage their juniors from going abroad, we hope they will give thought to the white-paper's correct statement that service overseas affords " opportunities to do interesting work in a new environment; opportunities to exercise individual initiative and responsibility at an earlier age than is usual here; opportunities to develop personal qualities of self-reliance, leadership and adaptability arising from the wide variety of tasks to be undertaken: opportunities to make an individual contribution to the development of a new country ". Even more, perhaps, we hope they will read the remarkable review of the African situation, by Dr. H. S. GEAR, which we publish this week. Though GEAR credits colonialism with having given Africa a phase of social stability with a rising economy, and recognises that the main medical contribution has been, and still is, made by the official services, he is concerned mainly with the unofficial aspects of a system which hitherto has been continually nourished and refreshed from Europe. " Medicine's true teachers and disciples give more to Africa," he says, " than medical care in a hospital or clinic ", and Western medicine should not overlook the need for this broader interpretation of its possible service. " It should guide Africa to create people who are good doctors and nurses, but are also prepared to follow fearlessly the principles founded over many difficult generations in Europe and America."

Protein in Hyaline Membrane

THE chief component of the hyaline membrane found on histological examination of the lungs of premature infants who have died shortly after birth was once believed to be inspissated material derived from the amniotic fluid or vernix caseosa; and the term " vernix membrane " was used for some years.[1] It now seems that a fundamental disorder of the pulmonary circulation plays a part in the formation of the membrane,[2] protein being extravasated from the pulmonary vessels into the neighbouring air-spaces and then forced by inspiration into a membrane lining the walls of these spaces.

While most agree that the bulk of the membrane is composed of protein, there is still some difference of opinion as to its origin and nature. LYNCH [3 4] initially suggested that the membrane represented a dried and concentrated secretion of the respiratory bronchioles and alveolar ducts. Further work indicated that the membrane included hæmoglobin,[5] but the bulk of it was composed of fibrin.[6 7] All these investigations reinforced the idea that the components of the membrane were derived from the blood-stream. The various cardiovascular factors associated with hyaline-membrane formation were analysed by SHANKLIN [8] in a series of 335 premature infants. He found that membrane formation was significantly more frequent in association with cardiac malformation that increased the pulmonary blood-flow. The stages of the development of the pulmonary lesion were thought to be increased pulmonary blood-flow, left ventricular failure, pulmonary œdema, and membrane formation. The possibility that maternal factors may play a part in the presumed circulatory disturbance has been investigated by COHEN et al.,[9] whose work seems to indicate that membrane formation is commoner when the pregnancy has been complicated by toxæmia and especially by antepartum hæmorrhage. From time to time it has been claimed that the frequency of hyaline membrane is increased in infants delivered by cæsarean section [10]; but COHEN et al. conclude that any such increase is limited to pregnancies where bleeding has occurred before delivery.

The composition of hyaline membrane has been investigated by BUCKINGHAM and SOMMERS.[11] They regard the structure as laminated acellular layers of eosinophilic material apposed to the walls of alveolar ducts, alveoli, and terminal bronchioles. Ultraviolet microscopy showed that the material closely resembled plasma-protein or cell cytoplasm; in addition, some nucleoprotein was thought to be present. Membranes produced experimentally by exposure of mice to oxygen had a similar composition. The membranes thus seemed to comprise cytoplasmic material, hæmoglobin, polymerised fibrin, nucleoprotein, and mucoprotein. These workers were impressed by degenerative changes in the bronchiolar epithelium, which they believe contribute to membrane formation. Hyaline membrane may possibly be associated with hypersecretion of alveolar lining substance [12]: which raises the question whether abnormal autonomic nervous stimulation enhances its formation, not only by promoting pulmonary œdema but also by increasing secretory activity in the terminal air-passages.

Although highly specialised techniques have revealed fibrin in hyaline membrane, this does not stain for fibrin by ordinary histochemical methods. It has been shown, however, that a hyaline material is formed when certain acid mucopolysaccharides react with plasma-proteins [13 14]; and the possibility that a similar mechanism may operate in hyaline-membrane formation has been investigated by CARONE and SPECTOR,[15] who induced pulmonary œdema in rats by means

1. Farber, S., Wilson, J. L. *Arch. Path.* 1932, **14**, 437.
2. See *Lancet*, 1958, ii, 945.
3. Lynch, M. J. G., Mellor, L. D. *J. Pediat.* 1955, **47**, 275.
4. Lynch, M. J. G., Mellor, L. D. *ibid.* 1956, **48**, 165.
5. Lynch, M. J. G., Mellor, L. D., Badgery, A. R. *ibid.* p. 602.
6. Gitlin, D., Craig, J. M. *Pediatrics*, 1956, **17**, 64.
7. Van Breemen, V. L., Neustein, H. B., Bruns, P. D. *Amer. J. Path.* 1957, **33**, 769.
8. Shanklin, D. R. *Arch. Path.* 1959, **68**, 49.
9. Cohen, M. M., Weintraub, D. H., Lilienfeld, A. M. *Pediatrics*, 1960, **26**, 42.
10. See *Lancet*, 1960, i, 686.
11. Buckingham, S., Sommers, S. C. *Amer. J. Dis. Child.* 1960, **99**, 216.
12. Pattle, R. E. *Proc. roy. Soc. B.* 1958, **148**, 217.
13. Walton, K. W. *Brit. J. Pharmacol.* 1954, **9**, 1.
14. Pappas, G. D., Ross, M. H., Thomas, L. *J. exp. Med.* 1958, **107**, 333.
15. Carone, F. A., Spector, W. G. *J. Path. Bact.* 1960, **80**, 63.

of α-naphthyl thiourea and then introduced, by the endotracheal route, various substances including dextran sulphate, nasal mucus, meconium, and concentrated amniotic-fluid suspension. All these substances contain acid mucopolysaccharides, and all produced a membrane which had similar tinctorial properties to those of the membrane found in the human lung and which also failed to stain for fibrin. This suggests that, if hyaline membrane is indeed largely composed of fibrin, then this is probably in a polymerised form. Similar membranes were also produced when these acid mucopolysaccharides were introduced via the trachea together with plasma-protein in animals not previously given α-naphthyl thiourea.

Even if the membrane is largely composed of fibrin, the reason for the chain of events leading up to fibrin precipitation in the lungs of some infants but not of others still has to be found. A possible clue is afforded by the work of LIEBERMAN.[16] As a result of preliminary studies he postulated that a deficiency of lung plasminogen-activator activity predisposed certain infants to hyaline-membrane formation. It could be objected that such a low enzyme activity might result from exhaustion of supply by the disease process itself[17]; but any such doubt has been largely settled by LIEBERMAN and KELLOGG,[18] who have now evolved an improved technique for measuring tissue plasminogen-activator activity. They describe their findings in specimens obtained from 61 fœtuses and newborn infants, comprising 15 cases of hyaline membrane and 46 controls. All but 2 (4%) of the control series showed plasminogen-activator activity, and none showed any inhibitor activity. By contrast none of the 15 membrane cases showed activity when lung cubes were examined, but in 2 out of 11 cases homogenised tissue showed some activity. The remaining 9 cases studied by tissue homogenisation showed no activator activity, and in 8 of them evidence of inhibitor activity was found. These results confirm the previous observation of defective plasminogen-activator activity in association with hyaline membrane. The inhibitor of the enzyme, found in most of the affected lungs, may explain the lack of success which has attended the therapeutic use of fibrinolytic agents in affected babies. In a preliminary communication in our present issue Dr. FLEMING and his associates at the National Naval Medical Center at Bethesda report apparent absence of plasminogen activator in the lungs of two men whose hyaline membrane followed "total body irradiation"; and their findings in dogs were consistent with the view that irradiation produces a potent inhibitor of activation. LIEBERMAN and KELLOGG suggest that, in infants, the enzyme defect may be genetically determined.

SETNIKAR et al.[19] suggested that an alveolar transudate is an essential part of amniotic fluid. If this is so, a rich source of fibrin is contained in the fœtal lung, and, if fibrinolytic activity is defective or absent, fibrin deposits may gradually accumulate and form into membranes after the onset of respiration. Again, deficient proteolytic activity in the lung may interfere with the alveolar lining layer and so affect the surface tension in the pulmonary air-spaces. Such an increase in the surface-tension is thought to promote atelectasis.[20]

Although much work is being done on hyaline membrane, it is abundantly clear that our understanding of its formation is still deficient; and no effective remedy is in sight.

16. Lieberman, J. *New Engl. J. Med.* 1959, **260**, 619.
17. See *Lancet*, 1959, i, 1234.
18. Lieberman, J., Kellogg, F. *New Engl. J. Med.* 1960, **262**, 999.
19. Setnikar, I., Agostoni, E., Taglietti, A. *Proc. Soc. exp. Biol., N.Y.* 1959, **101**, 842.

Troubled Families

"... the State's principal duty is to assist the family in carrying out its proper functions."

So say the Ingleby Committee whose report,[21] published last week, gives important and far-reaching advice on means of helping delinquent, disturbed, and neglected children under 17. Unfortunately cause and prevention did not enter into their terms of reference, but it is clear that the committee believed that the family and the relationships therein were the primary causes of later difficulties, whatever secondary influences may subsequently play a part—an emphasis which colours the recommendations throughout. The parents, as much as the disturbed child, need to alter their ways, and the committee have wisely regarded the child as a person to do things *round* rather than the patient or sinner to do things *to*.

Set up by the Home Secretary in 1956, the committee[22] record that at that time falling delinquency-rates and fewer maintenance and affiliation orders set a scene which, if not rosy, was at least hopeful. But since then this trend has been dramatically reversed, so that the Ingleby recommendations gain much in significance and will be given prompt Governmental scrutiny.

Considering first the ways in which help reaches the family, the report notes that inter-service rivalry has, in the past, impaired coordination and delayed the arrival of appropriately trained workers. Thus, while the committee welcome the help of almost any agency in bringing troubled families and children to notice, diagnosis and treatment require tactful handling and, very often, special skills not always found among those who concern themselves with the personal affairs of others. A reorganisation of the various family services is called for, with the establishment of an independent "family bureau" responsible only to the clerk to the local authority. Detailed consideration of local-government changes was beyond the committee's terms of reference and they urge further study of this matter, bearing in mind that differing local circumstances will call for flexibility in legislation designed to ensure efficient coordination. The report declares that "... there

20. Avery, M. E., Mead, J. *Amer. J. Dis. Child.* 1959, **97**, 517.
21. Report of the Committee on Children and Young Persons. Cmnd. 1191. H.M. Stationery Office. Pp. 179. 8*s*.
22. The members were Lord INGLEBY (chairman), Lady ADRIAN, Hon. Mrs. P. L. AITKEN, Mr. R. H. BLUNDELL, Mr. DONALD FORD, Dr. R. M. JACKSON, Mrs. M. M. C. KEMBALL, Mr. G. H. MCCONNELL, Prof. ALAN MONCRIEFF, Viscountess RIDLEY, Dr. P. D. SCOTT, Mr. G. A. WHEATLEY, Alderman D. T. WILLIAMS, and Mr. J. P. WILSON.

should be a general duty laid upon local authorities . . . to prevent or forestall the suffering of children through neglect in their homes," and such authorities should be required to submit schemes for Ministerial approval. The only bodies, the report goes on, with the power to bring a case before the courts should be the police and the local authority—a move, it seems, away from the sometimes harmful multiplicity of authorities bearing on the family. This proposal, which removes such power from the National Society for the Prevention of Cruelty to Children, is likely to be a contentious one when debated in Parliament and elsewhere, but it is in tune with the legitimate trend towards professionalism in social work. The days of the keen but untutored amateur are passing, and rightly so. The reluctance of the committee to widen " juvenile liaison schemes ", run by the police for cautioned offenders, springs from similar judgment.

Turning to jurisdiction, the committee note the trend, over the past century or so, towards separate provision under the criminal law for the young and, more and more, towards emphasis on the welfare of the child as the overriding concern. This has led, the committee believe, to inconsistencies. The principle of criminal responsibility and punishment for a certain act in a judicial setting has become uncertainly combined, by statute, with the obligation to serve the child's best and broadest interests. Thus a trivial offence may, when the full appalling family circumstances become known to the court, lead to a seemingly severe and drastic disposal. Furthermore, the widening of the court's function in 1908 and 1933 permitted a child to be sent to an approved school (a severe punishment very often) for the non-criminal offences of being " beyond control " or in need of " care or protection ". In rethinking the place of juvenile courts the committee concluded cautiously that, however much a child may seem likely to benefit from interference by the State, compulsory intervention should not be applied except for the clearly defined and well-known reasons that already obtain. The basic pattern of courts, too, with lay justices still finds favour with they committee, though they concede some virtues to the non-judicial tribunal.

The trend away from criminal jurisdiction, however, should be urged forward, notably by raising the minimum age of criminal responsibility from 8 to 12 years, and later perhaps to 13 and 14. Though an important change of principle, the practice of the law would not be as much affected by this as might be imagined. Already offending children under 8 may be brought before a court and dealt with as " beyond control ": the court, under these proposals, will certainly not allow children to " get off "; indeed by the greater thoroughness of the procedure, Society may expect better protection than before. Children under 12 would no longer be charged with an offence, though if such were established (under the usual rules of evidence) it would count towards showing that the child was " in need of protection or discipline "—the new form of words empowering the court to take action. The procedure would be swifter (cases would have to be tried within 28 days of detection, save in special circumstances) and more holistic, taking in the whole circumstances of the case. The police and local authority would consult before proceedings began. Though retaining the power to remove a child from home, the court would do so only when it was satisfied that his needs could not be somehow met without such action, and it would have the additional options of ordering attendance at an attendance centre or study in a remand home. Fines and detention in detention centres would be withdrawn, but compensation to a maximum of £100 and/or costs could be demanded. Committal to the care of a " fit person " would remain, and parent or guardian could be ordered to enter recognisance to exercise proper care and guardianship. The court could also order supervision by a probation officer or other person for up to 3 years. From 12 to 17 years procedure would be much as it is now, and the committee did not feel that the age-limit of 17 for juvenile courts should be raised, though they wondered whether a sort of half-way " youth court " for ages 17 to 20 or 21 might be examined further.

The committee believe that the court needs to be much more active with the parents, summoning the attendance of both, bringing home to them their share of responsibility, and offering support where it is practicable. The verdict of the court—so often a source of grievance—would be explained to them as far as possible. Treatment, where compulsory, appears as punishment, and the committee admit that in practice it is impossible to distinguish between them. On the other hand, parents would no longer have the right to bring children before the court as " beyond control ", though appeal to the local authority might sometimes have the same effect if no other solution could be found. Here, however, parents would not appear in the role of prosecutor, and the need for them to make damaging and rejecting statements towards the child in public would be reduced.

The greater part (some 400 out of 550 paragraphs) of the report is a review of administrative detail arising partly from this survey and related to courts, sentences, and corrective institutions. Few of the numerous recommendations will be disputed; nor are many of wide interest, important though they are. Thus, an adequate course of training is recommended for all juvenile-court magistrates, who should usually be lay people, appointed between about 30 and 40 and retiring at 65. Better court-room accommodation for the children is needed; and the report calls for removal of all legal obstacles to accelerate the disposal of cases involving child witnesses, plus closer liaison with adult courts where necessary. The committee approved the attendance-centre principle sufficiently to want to lower the minimum age to 10 and to widen the categories of offenders treated there. For detention centres, however, a uniform 3-month sentence should take the place of the present sliding scale between 1 month and 6 (for under 17s only), and the committee are surely right in pressing for compulsory aftercare for a further 6 or 12 months.

Approved schools are left much as they are, with a few hopeful calls for inter-school staff discussions and better psychiatric facilities, staff, and aftercare. Recent months have made it clear that all is far from well among the approved schools, but from present knowledge it is hard to see how the committee could go further than they have, timid though their recommendations seem. Finally, the committee want to extend somewhat the prosecution of cruel parents (to take in mental suffering short of actual derangement) and to increase the penalties to £100 or 6 months' imprisonment or both, though at the same time full use should be made of residential training and social aid.

In sum, these proposals do not seem to conflict with any of the many other Governmental reflections of recent years; and they all have it in common that the big problem in realising them is shortage of staff and money. (We have now heard from so many committees that a "survey of reports" might help to place the future of our social services in comprehensive perspective.) There is little of dynamite in the Ingleby recommendations. Juvenile-court organisation, in particular, has been left largely alone, to the disappointment, undoubtedly, of many. But the committee have reached a quite surprising degree of unanimity after their 4-year pilgrimage, and few who advocate sweeping changes have given such careful thought to the implications. These proposals, in the present state of therapeutic knowledge, are probably as far as we should go and must carry an excellent chance of early Parliamentary acceptance. Coming when voluntary acceptance of child and family guidance services is spreading and when compulsory treatment for "psychopaths" is becoming possible under the National Health Service, we have now the foundations of an excellent service for children. The wisdom of this report cannot be in doubt; and the sooner it all happens, the better it will be for everyone.

Annotations

SOCRATES IN HARLEY STREET

SOME two years ago, in a week when medical education was being considered at a formal conference in London, we printed a less orthodox discussion of the same problems in our peripatetic columns. It began:

ALCIBIADES: Tell me, Socrates, how can we be sure that our doctors are well trained?

SOCRATES: Do you think it right, Alcibiades, that we should say of a pudding that it is good or bad?

ALCIBIADES: Certainly, Socrates.

SOCRATES: It must be possible then to distinguish a good pudding from a bad one?

This learned ballon d'essai pleased readers, author, and editor. Socrates was offered a column of his own, and throughout 1959 under the heading of "Dialogues of Today" he and his disciples debated in our columns some of the social and moral uncertainties of medicine and humanity, of our time and all times. Because the dialogues deal with problems which belong not only to medicine and not only to this country, we have reprinted them as a small book (with paper covers)[1] for the consideration of all who enjoy a good argument.

The dialogues range from birth control to death control, from ways of constituting a committee to the reasons for constituting a college, from the atomic bomb to less final methods of retirement. But if the matter is serious the manner is never heavy. No dogmatic conclusions are offered and the reader is left to continue the debate with his own friends—and perhaps with himself. The anonymous author admits that he has chosen the conversational form with provocative intent. His introductory quotation, borrowed from David Hume, another writer of dialogues, describes dialogue writing as peculiarly suitable for a topic which is obvious but important or for one which is so obscure and uncertain that the human reason can reach no fixed determination with regard to it. "Reasonable men," Hume adds, "may be allowed to differ, where no one can reasonably be positive. Opposite sentiments, even without any decision, afford an agreeable amusement." We hope that all our reasonable readers will find agreeable amusement with Socrates.

1. Socrates on the Health Service. 1960. London: THE LANCET Ltd. Pp. 102. 5s. Obtainable from THE LANCET, 7, Adam Street, London, W.C.2 (postage 5d.).

CHOLESTATIC VIRAL HEPATITIS

EVEN before the 1939–45 war it was recognised that a varying but small proportion of cases of epidemic viral hepatitis differed from typical cases in the difficulty with which they could be distinguished from cases of extrahepatic biliary obstruction.[1] Histologically the liver in such cases was characterised by the extreme mildness of the parenchymal lesions and their restricted focal distribution; the conspicuous features were multiple intralobular plugs of bile and moderate to severe infiltration of the portal tracts with both mononuclear cells and polymorphs. Hitherto deviation from the more usual pattern of the disease has not been satisfactorily explained.

Dubin et al.,[2] on the basis of their experience at a U.S. Army Hospital in the years 1951–53, suggest that the cholestatic form of hepatitis may be due to a variant of the usual virus. Their clinical material comprised 93 cases of viral hepatitis in which biopsy of the liver was undertaken within twenty-one days of the onset of jaundice. By means of clearly defined criteria these cases were classified into four types. Type A showed the diffuse necrosis with very slight bile stasis that is typical of classical viral hepatitis. Type B was similar, but intralobular plugs of bile indicated some added cholestasis. Type C was characterised by focal distribution of the parenchymal lesions and predominance of cholestasis. In type D parenchymal necrosis was negligible, the changes consisting almost entirely in bile stasis and cellular infiltration of the portal tracts. Patients with lesions of types A or B were regarded as having classical viral hepatitis; and those with lesions of types C or D as having the cholestatic form. When the cases were classified into serum hepatitis and infective hepatitis according to whether or not the patient had received a transfusion of blood or blood product in the six months preceding the appearance of jaundice, correlations appeared between serum hepatitis and the classical picture

1. Eppinger, E. Die Leberkrankheiten. Vienna, 1937.
2. Dubin, I. N., Sullivan, B. H., Le Golvan, P. C. Murphy, L. C. *Amer. J. Med.* 1960, **29**, 55.

and between infective hepatitis and the cholestatic form. This, however, was contrary to the results of all previous studies, and further analysis showed that the more probable correlation was between the variety of the disease and the area where it was contracted. Thus of the 36 patients with serum hepatitis, of whom only 5 belonged to the cholestatic group, 30 had been transferred with their disease from the Far East; whereas of the 54 patients with infective hepatitis, of whom 21 belonged to the cholestatic group, only 8 were from the Far East and 46 were of local origin. All 21 cases of cholestatic hepatitis occurred among the 46 local cases of infective hepatitis: which suggests that the local epidemic virus had a remarkable predilection for inducing the cholestatic form of the disease. Since no other factors, such as exposure to drugs or toxins, were apparently responsible for this distribution of the cholestatic form, Dubin et al. feel justified in attributing it to some special property of the virus. The even higher incidence of this form in the epidemic in Delhi described by Smetana [3] can be taken as evidence of widespread distribution of this variant of the infective-hepatitis virus.

THE GENE

IN a British Association Granada lecture delivered in London on Sept. 27, Dr. G. W. Beadle, professor of biology at the California Institute of Technology, surveyed mechanisms of heredity. There seems to be no doubt that it is the cell nucleus that contains the primary hereditary message, the gene being the simplest unit of biological instruction, and some 10^4–10^6 of them being necessarily present in every human egg. The only nuclear constituents of sufficient complexity to carry such a message are the proteins (linear polymers of some 20 different amino-acids) and the desoxyribonucleic acids (D.N.A.) (linear polymers of only 4 different nucleotides). Evidence favouring D.N.A. as the carrier arose initially from the demonstration that bacterial transforming factors (which cause a typical inherited change in some pneumococci) were composed almost entirely of D.N.A.,[4] but perhaps the most direct proof came from a study of a bacterial virus with inheritance characteristics known to be particulate. These bacteriophages consist of a protein coat surrounding a core of D.N.A., and electron microscopy had suggested that the protein coat did not enter the cell during the process of infection. The protein coat was therefore labelled with ^{15}N and the D.N.A. with ^{32}P, and it was conclusively shown that only the D.N.A. entered the cell. Thus since these viruses have genes, and since only viral D.N.A. entered, the viral genes must be D.N.A.

The double-stranded D.N.A. molecule,[5] where the sequence of nucleotide units in one strand automatically determines the complementary sequence of its partner, gave a clear indication of how accurate replication could occur provided that sufficient energy was available to separate the two strands by some sort of untwisting process.[6] There is certainly enough D.N.A. in a single human egg to carry all the required information; for about 10^{10} nucleotide units exist in the 46 chromosomes of the fertilised egg (ignoring the sex chromosomes), and such a number is probably sufficient to encode the contents of some 500 large books.

The gene, then, can be thought of as a segment of the D.N.A. chain, perhaps some 1000 nucleotide pairs in size, and the process whereby such a gene may direct the synthesis of an enzyme involves transferring the code to ribonucleic acid (R.N.A.) (known to be associated with the chromosomes at certain times) by some kind of template system. The nuclear R.N.A. then passes to the cytoplasm, where it becomes incorporated into the microsomes. Special segments of this R.N.A. bind and activate specific aminoacids, which are thereby held in the correct order for the synthesis of the particular enzyme. This type of synthesis probably occurs only when the enzyme substrate is present—so providing a necessary control to prevent every cell from undertaking all possible syntheses. In this way differentiation may be controlled by environment. A clear example of such genetic control of enzyme synthesis is the inherited condition of galactosæmia, where the patient wholly lacks the enzyme which changes galactose into a usable form.

Mutations can be thought of as alterations of the sequence of nucleotides in the genic D.N.A. either chemically (for example, nitrous acid changes D.N.A. amino groups into hydroxyl groups and so upsets the hydrogen bonding on which accurate replication is thought to depend) or spontaneously under the influence of natural radiations. Only occasionally, however, does such a mutation lead to an organism of increased reproductive fitness and so to a permanent evolutionary change.

Professor Beadle ended by suggesting that paths now seem open, beginning with a universe of hydrogen, to an evolution through other elements, simple inorganic and then organic compounds, then through more complex organic systems to polynucleotides and proteins, the simple virus-like molecules, simple cellular systems, and finally to man himself.

FROZEN BLOOD FOR TRANSFUSION

THE Cohn fractionator [1] is designed to separate individual half-litre units of blood into the component parts—red cells, platelets, and plasma—and to wash the red cells free from plasma. It consists of a bowl centrifuge whose temperature can be kept constant, and whose bowl and associated containers can be sterilised. Haynes et al.[2] have been using this machine for the long-term preservation of blood for transfusion. The cells are washed with solutions containing up to 50% glycerin, then frozen at −80°C or −120°C, and after storage for 1 to 44 months thawed, deglycerinised, and reconstituted with an appropriate diluent. According to requirements, the cells can be resuspended in saline, their own serum which has also been frozen, or 5% human albumin in an isotonic salt solution, to which can be added, as needed, buffers, globulin fractions, or components of clotting systems. Of the red cells taken from the donor, 82% reach the recipient, and these seem to survive in his circulation as long as fresh cells. Results have been so satisfactory that this frozen and reconstituted blood has been in routine use at the U.S. Naval Hospital in Chelsea, Mass., for more than a year. So far over 1000 units have been administered without trouble; Haynes et al. remark that febrile reactions have been remarkably few, and hepatitis has been absent.

The cost of these benefits is considerable. Rough costing suggests a figure of about £6 per unit, excluding

3. Smetana, H. F. *in* Hepatitis Frontiers. Boston, 1957.
4. Avery, O. T., McLeod, C. M., McCarty, M. *J. exp. Med.* 1944, **79**, 137.
5. See *Lancet*, 1959, ii, 655.
6. Watson, J. D., Crick, F. J. C. *Nature, Lond.* 1953, **171**, 964.

1. Cohn, E. J. Proceedings of the fourth annual meeting of the American Association of Blood Banks, 1951.
2. Haynes, L. L., Tullis, J. L., Pyle, H. M., Sproul, M. T., Wallach, S., Turville, W. C. *J. Amer. med. Ass.* 1960, **173**, 1657.

building and heating; and a team of six workers using two fractionators can process only 200 units monthly. Many London hospitals, dealing with 15,000–20,000 inpatients a year, may need over 500 units of blood in a month. This would call for five fractionators and a team of twelve or fifteen, besides the existing staff of two technicians and a part-time doctor. The cost of each bottle of blood for transfusion would rise from the present £1·25–1·5 to something like £6–7. Further, such hospitals use blood chiefly to treat unexpected hæmorrhage; relatively little blood is used for elective surgery or for the treatment of anæmia; so a large supply of fresh, or already reconstituted, blood would have to be kept on hand. Now that the incidence of post-transfusional hepatitis has been reduced to 1 in about 800 transfusions, there seems to be little point in providing this expensive equipment for individual hospitals.

On the other hand, there may be a case for setting up a few processing units for blood of unusual groups. Very rare red cells, such as -D-, could be reserved against need, and a moderate stock of blood of the less common groups which may be needed for extracorporeal circulations could be established. In the past few months, because many regular donors have been on holiday, there has been a shortage of blood of all kinds,[3] which fortunately has led to nothing more serious than the postponement of elective operations for a week or two; it might be possible to store blood collected in the autumn, winter, and spring against the needs of the summer. But such a project is bound to be expensive, and it is doubtful whether it would produce more benefits than would half the money spent on something else.

SHINGLES AND CHICKENPOX

Wesselhoeft,[4] in delivering the sixteenth Charles Value Chapin oration, took the opportunity to review past and present ideas about the nature of chickenpox and shingles, and gathered into a valuable bibliography accounts of experiments and observations from many sources. Those who thought that Weller and Coons [5 6] in the laboratory, and Hope-Simpson [7] in the field, had convinced the medical profession of the unitary nature of varicella, however contracted, may be disappointed by the note of agnosticism on which he ended his address.

The journals tend to give more space to rare than to common events, and this predominance may disturb the balance of a comprehensive review. Rare occurrences are informative and must not be dismissed; but, still less, the common pattern of behaviour of a disease should not be overlooked. There is a real danger of missing the wood for the trees, especially rare trees.

The common relation between shingles and chickenpox is as follows. Both can cause chickenpox in susceptible contacts, though the risk of this happening after contact with shingles is less than a third of its happening after contact with chickenpox. In either case the resultant disease is, by clinical, epidemiological, and virological criteria, ordinary chickenpox. On the other hand, neither chickenpox nor shingles gives rise to an attack of shingles in contacts, whatever their previous history of either disease. This is the usual pattern shorn of rare exceptions, and it determines the epidemiological behaviour found in practice—namely, that chickenpox appears in epidemics when aggregations of susceptible persons are effectively exposed to cases of chickenpox or shingles, but that shingles does not itself appear in epidemics and is independent of epidemics of chickenpox.

For the " dualist " who holds that there is a distinction between ordinary and zoster-induced varicella there is a difficulty that seems never to have been adequately considered. How far backwards must the antecedents of a case of chickenpox be traced before it can with certainty be classified as " ordinary " and not " zoster-induced "? Are ten generations of ancestry to be considered adequate evidence, or a hundred, or a thousand? One observer traced back an outbreak for twelve months and classed it as " ordinary varicella ". Had he, by pushing the inquiry still further into the past, found that the outbreak in fact stemmed from an original case of shingles, he would have been compelled to reclassify it as one of " zoster-induced varicella ". Except in remote areas it is seldom possible to back-track in this way with any certitude, and, in such remote regions, outbreaks are commonly found to stem either from a local case of shingles or from a case of chickenpox imported from more crowded areas where further investigation of the lineage of the virus is difficult. On all the evidence, it should surely be conceded that there is only one chickenpox, which can be caught either from another case of chickenpox or from a case of shingles.

Much remains to be understood, foremost the nature of shingles itself. If, as seems likely, it is due to the reactivation of latent chickenpox virus, where in the body is the latent remnant? Do all who have had chickenpox depend upon the survival of this latent brood for the preservation of their immunity? How is the symbiosis disturbed so that a harmony of maybe fifty years breaks down, the eruption develops in a dermatome, and infectious chickenpox virus escapes into the environment? On questions such as these light may be shed by the more unusual happenings, the anomalies and exceptions to the common pattern described above. The least uncommon anomaly is the occurrence, usually in children, of a zoster during a primary attack of chickenpox—an apparent exception to the rule that contact with chickenpox does not give rise to shingles. Much rarer are those cases in which shingles in an adult appears to have been caused by contact with another case of shingles or a case of chickenpox. How uncommon this is was shown by a prospective study of thousands of contacts of cases of chickenpox and shingles of whom not one developed shingles. Nevertheless cases have occasionally been recorded in circumstances that make them very unlikely to be fortuitous. Again there are a few records of attacks of zoster-induced varicella failing to protect against subsequent exposure to chickenpox. All such rarities must find their explanation in a more complete understanding of the two diseases, but in the meantime they should not be allowed to obscure the picture which is already emerging.

Even if some laboratory refinement should in the future discover a recognisable peculiarity of virus newly released by an attack of shingles from its intracellular confinement, the interesting observation would no more disturb the ætiological picture than a similar finding in spirochætes from late cases of syphilis would unsettle our present conception of that disease.

3. See Graham-Stewart, C. W. *Lancet*, Aug. 20, 1960, p. 421.
4. Wesselhoeft, C. *R.I. med. J.* 1957, **40**, 387.
5. Weller, T. H. *Proc. Soc. exp. Biol., N.Y.* 1953, **83**, 340.
6. Weller, T. H., Coons, A. H. *ibid.* 1954, **86**, 789.
7. Hope-Simpson, R. E. *Lancet*, 1954, ii, 1299.

The Wider World

MEDICINE AND THE NEW AFRICA *

The Passing of Colonialism South of the Sahara

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Africa south of the Sahara forms a unit of countries with many common features. Because of early remoteness, climate, and disease, it was until lately isolated from Europe, and so lacks written history. Its peoples—Bantu, Negro, Hamite—have many common physical and social characteristics. It is the Africa of the tropics and semi-tropics, with desert, jungle, heat, and sun obtrusive. It has been the region of the world most affected by European colonialism. It has had an evil name because of the men, especially those coming from temperate lands, who have been killed or disabled by its sicknesses.

European influences were first brought to the continent by explorers, missionaries, traders, and prospectors. In the 19th century the Colonial Powers, scrambling after them, launched tribal Africa into the Western way of life, and brought it precipitately into the material and technological world created by the Industrial Revolution. Through the colonial agents of this world phenomenon, Africa was in time largely freed from the blight of tribal massacres, slavery, starvation, and epidemic disease.

Today Africa is impatiently grasping the outward forms of sovereignty. More than half her peoples will achieve political independence this year, and before the decade is well advanced the rest will almost certainly have followed. Colonialism will then have vanished and new, and largely inexperienced, States will be struggling with the daunting social problems of emerging millions. This fact, partly political though it may be, directly affects the future of medicine in Africa.

The astonishing reduction in the amount of disease during the past 60 years has been possible because colonialism gave Africa a phase of social stability with a rising economy, and the whole paraphernalia of good central and local civil administration. Western medicine had then its opportunity to prevent and cure disease "en masse".

Western ideas have moulded the form medicine has taken both in sovereign countries like the Union of South Africa and the Federation of Rhodesia and Nyasaland, as well as in the Colonial territories of Belgium, France, Portugal, and the United Kingdom. In this medicine there has been a significant place for the medical missionary, the private practitioner, the medical professional association, the autonomous university with its medical school, and the public but unofficial research institution. It has been a medical system constantly nourished and refreshed from the European home countries.

But, though this European form of medicine has given a place to the non-governmental and the non-official, most medicine in Africa has a strong official character. The hospital and clinic services of South Africa and the Federation and the general Colonial Services, despite their Western origin, are largely official and depend on Government funds for providing free or subsidised services.

If the future held no other obstacles, the official nature of most of the developing African medical systems would create difficulties enough. This official bias will be continued by most forms of external aid. It makes uneasy those who would like to see the individual doctor and the non-official organisation claim a worthy place.

Medicine, in a full sense, today only achieves results if there is an adequate community with law and order, efficient civil administration, good communications, and a sound economy. In other words the good health of a community needs not only good doctors, but also well-run cities, villages, and country districts with sufficient food, pure water, efficient waste-disposal, proper housing, and all the other advantages of good government. Inevitably the changing political and social scene in Africa will alter the future of medical and other public services.

UNITED NATIONS AID

The New Africa is being moulded by external as well as internal forces. The most important stimulus comes from the United Nations family, with the World Health Organisation as the agent responsible for health and medicine. It is perhaps not fully realised how great a change is being wrought by the United Nations agencies, even though they are intergovernmental and not super-governmental organisations.

Delegates from African States appear in ever-growing numbers in the councils of the world and many already have been effective office-bearers. African regional and other offices already represent the U.N. Economic Commission for Africa, the U.N. Technical Assistance Administration, the Food and Agriculture Organisation, the World Health Organisation, and the U.N. Children's Fund. Most of these directly or indirectly affect health programmes, and as a group are not insignificant in power and resources.

A stream of people—consultants, technical experts, advisers, and others—are being directed by the U.N. group into Africa. Another stream flows out carrying delegates, committee representatives, and postgraduate fellows and students.

People moving in and out of Africa as part of its technical and scientific evolution are not a novelty. But there is something very different about the flow sponsored by the United Nations family. The volume is more impressive and it is directed to and from many more countries. U.N. consultants and technical experts now working in Africa come not only from the United Kingdom, France, and the other colonial countries, but from North and South America, the whole of Europe, and several Asian countries. The Africans travelling overseas for experience and training also visit a much wider range of countries.

The technical aid in medical fields is massive. It is gladly accepted by the new African States without the undue sensitivity they sometimes show to aid offered by individual foreign Governments. As a result, the organisation of hospital services and clinics, and the training of doctors, nurses, and other staffs have been speeded up.

A fundamental principle in this form of external technical aid is to be noted. Since the United Nations system is official and intergovernmental, it works through national governmental services. It is thus a force which quite properly creates and strengthens official and governmental services in the countries it helps. It is supporting officialdom everywhere, and will increasingly do so in the future African medical and other services. This is satisfactory provided non-governmental organisations and arrangements are not neglected.

* Based on a lecture delivered under the auspices of the Institute for the Study of Man in Africa, Johannesburg, on June 14, 1960.

OTHER INTERGOVERNMENTAL ARRANGEMENTS

The passing of direct colonial control and the arrival of United Nations technical aid do not mean that the Colonial Powers have given up all responsibility for emerging Africa. They are helping in the development of such things as general administrative services, universities, hospitals, rural clinics, research institutions, water-supplies, and roads. Their hope is that if the new countries have sound public services the transfer of authority to peoples who, though politically active, are on the whole administratively and technically inexperienced will be smoother.

It is not only the old Colonial countries which are eager to help the New Africa. The Union of South Africa has often and officially stated that it wishes to draw on its own rich technical resources to help the rest of Africa. Such help has already been given in many ways:

Several South African scientists have visited other African countries; some have served as consultants; a few students from other territories have been trained in the Witwatersrand, Cape Town, and Durban Universities and medical schools; some research teams have worked on general African problems; and the South African Institute for Medical Research is used by many medical services as far away as the Sahara. It is also part of several international scientific networks—e.g., in virus diseases, spirochætal infections, bilharziasis, malaria, and so on.

However, it is doubtful if South Africa yet plays a part proportionate to her technical resources. Compared with the many scientists and doctors working in the New Africa who have come from Britain, France, and other European countries, or with the hundreds of undergraduate and postgraduate African students who flock to other medical centres, South Africa seems inactive. Yet unless she vigorously develops this two-way exchange of medical scientists and students, her own medicine and science may languish as an international or African force.

A more recent feature of intergovernmental technical aid to Africa is the bilateral governmental system. Its first great advocate was the United States of America, and Africa has benefited liberally. American medical missions are important now in many African states, and there is a steady stream of African students to the great medical and public-health schools of the United States. She is keen, too, to cooperate with local groups in research into the many tropical and other diseases which are still difficult to control or treat such as bilharziasis, malnutrition, and many parasitic conditions.

But the American bilateral programmes are having some unexpected imitators. The Communist countries are already at work in many fields, including medicine, and it is probable that the Chinese will also join in sending technical experts and attracting fellows and students from the African States.

NON-GOVERNMENTAL INFLUENCES

The pioneers of Western medicine in Africa, as elsewhere, were not officials but private doctors, and the medical missionary was the pioneer of the pioneers. For a hundred years these courageous and selfless people have been among the great medical and social liberators of Africa. Their work, generous and independent, goes on. Today it is perhaps again critical. If tolerated in the new countries, these societies could be a valuable instrument in continuing the spirit and practice of personal and non-official medicine of the best type.

It was earlier inevitable, in tropical and tribal Africa, for the Colonial Powers to break the shackles of epidemic and endemic disease by introducing modern medicine through official services. So, with the important exceptions of the larger European communities, the private doctor has not been a force.

Again, with the exception of South Africa and Southern Rhodesia, medical and nursing professional associations have had an insignificant influence on medical and health policies in Africa compared with the part they have played in Europe and America. The professions are generally a sound influence on official ministries, for in considering national health problems they usually hold more than a narrow professional view. They contribute wisdom and experience and usually add to the maturity of the community. It is, therefore, unfortunate that strong professional associations with a backbone of independent doctors seem unlikely to develop in the newer African States.

Yet, paradoxically, one of the dangers threatening medicine in Africa is the private doctor who abandons the ethical code of his profession. The charlatan in Africa is already playing on the credulity of the naïve and superstitious. He may be witch-doctor, masquerading doctor, or qualified practitioner prostituting his calling. The new States, therefore, have a clear responsibility to protect their people from exploitation. But the State will not succeed in this aim without a medical profession of the highest integrity keen to keep its own house in order.

Industry has also contributed to African medicine. Most large industrial organisations have acknowledged their obligation to protect the health of their communities. In the gold, copper, and trading industries of South Africa, the Rhodesias, the Congo, and West Africa hundreds of thousands of workers are given health and good physique and learn much about keeping themselves fit during the years of their employment. Much of this knowledge diffuses into the kraals and villages. Hence the position of industry in the new States is of concern to medicine. If they accept that private industry can contribute to the economy, this will open a useful opportunity for non-governmental medicine.

Another non-governmental agent which could do immeasurable good for medicine in the New Africa is the large philanthropic or public Foundation. In Africa the Rockefeller and other American foundations have been joined by the Nuffield Foundation, whose support for the establishment of a vigorous and modern medical school in Salisbury is likely to be one of the germinal events in Central African medicine. As Africa changes from colonialism, the great Foundations, both American and British, will have an opportunity of service greater than in the past. They are altruistic, objective, generous, and free of politics and bureaucracy. They thus can balance the help coming to Africa from the intergovernmental agencies—multilateral or bilateral—with the best type of non-governmental support. It will be unfortunate if the new States are unwilling to invite the Foundations to help in the large new medical, technical, and social programmes for which they will soon be responsible.

A final example of non-governmental health and medicine is the voluntary organisation. In South Africa and the Rhodesias, and to a lesser extent in the Colonial Territories, such bodies have been valuable, and it is to be hoped that the New Africa will encourage the work of voluntary groups, particularly in child and maternal health, first-aid, accident prevention, and social welfare. But many circumstances are against them, especially if the new States loosen their Western relationships.

SOCIAL TRANSFORMATION

The New Africa to which medicine must adjust itself is as much a product of social, including economic change as of the more obvious political movements. These social changes—in such things as education, economy, agriculture, industry, science, and communications, and in religion—have been accelerated by the results of Western medicine. The reduction of pestilence, as much as the control of famine and tribal warfare and the abolition of slavery, launched the African social revolution. Now, along with the present political and nationalistic movements, these social forces are influencing the future setting for African health and medicine. Indeed the replacement of the social customs of tribal Africa, by something modelled on, or influenced by, external ideas and examples, is happening too rapidly for medicine and the other social services to keep pace. Even if these social forces are not diverted or delayed by political troubles, medicine in the New Africa will still have to face problems very different from the old.

One is already ominous—the growth of population. Released from the old checks of slavery, starvation, tribal war, and preventable disease, the annual rate of increase in some territories is already 3%. People are migrating into the towns and factories, and large urban and industrial populations may place an unbearable demand on public, including medical, services. The witch-doctor is no longer supreme. Old fears have gone, so that hospitals and clinics are being swamped, and overworked doctors and nurses are driven to exhaustion. Africa, like most other developing countries, has too many ugly and squalid towns and villages, and yet their inhabitants increase relentlessly to make slums more depressing and dangerous. Only watchful sanitary administration and good fortune seem to explain the relative absence hitherto of serious disease.

Another feature of the social transformation of importance to the medical reformer is the growing emancipation of the African women. In much of Bantu society women still lack freedom and are only slowly training as midwives, nurses, health visitors, or teachers. Sufficiently educated girls are deplorably few to meet the urgent demands of nursing and teaching.

CHANGING PATTERN OF DISEASE AND DISABILITY

Africa's reputation has not yet recovered from the casualties among those who in earlier days came to explore, trade, or fight. Portuguese missions defeated by fever; Mungo Park's expedition ending in disaster; Dutch, Danish, French, and British trading-posts on the West and East coasts enlarging their cemeteries daily; the decimation by typhoid and dysentery of the South African, and by the malaria and dysentery of the East African campaigns of the first world war—these and many more gave a sinister name to the climate and disease of Africa.

Before medical science unravelled the maze of tropical disease, the hazards of Africa seemed to lie in its malignant climate. Sun, swamp, heat, miasma—all were accused. However, recognition of the true situation has seen the dramatic conquest of most of Africa's pestilential and tropical diseases. Not only is the indigenous African population doubling itself every 30–40 years, but European families are living happily and healthily even in such dreaded areas as the West Coast and the Central African Valleys. If one of the 18th or 19th-century Europeans returned, he would perhaps be chiefly amazed by the contempt of the moderns for the huge pith helmet, red spinal pad, and abdominal or cholera belt which he considered an essential protection against the baleful African sun and climate.

Today we have gone a long way towards separating the climatic and environmental from the communicable and nutritional factors in the cause of African disease. The greatest triumphs were the discovery of the causes and methods of treatment and control of the tropical fevers. The devastating epidemic and endemic diseases of previous centuries are now cowed. Yellow fever, malaria, sleeping-sickness, smallpox, dengue, yaws, and many more are shadows of their former selves. The blame placed on tropical and African climate is now known to have been much exaggerated. Now we know that an efficient sanitary system and a good diet can make nearly all Africa tolerable and healthy.

Formerly nearly all the dangers to life lay in communicable disease carried by insects or infected food or water. Climate was indirectly responsible in that it gave these diseases the medium for their propagation. With disease reduced or eliminated, tropical climates become themselves less fearsome, if still uncomfortable. Today we know much about the direct effects of sunlight, heat, and humidity. Unpleasant though extremes of these may be, their effects can be borne more tolerably by applying the present knowledge of the human body's capacity for acclimatisation and adjustment. Much of this work was shown on the Witwatersrand—e.g., the regime of adjustment to work, environment, heat, and humidity applied in the mines. The human power of physiological adaptation, combined with modern housing and work places, and, if necessary, air-conditioning, is radically changing the medical view of the future capacity of Africa to support healthy human populations even in its more fearsome desert and jungle regions.

With the astonishing decline of the pestilences a new pattern of diseases is appearing. Some of these diseases have always existed but were overshadowed. Others seem to be truly new, or much more virulent. Others are a product of social change.

Examples of diseases now more prominent by contrast are malnutrition and some of the dysenteries. Mass famine is now rarely seen, but protein malnutrition has lately been recognised as widespread. Infantile diarrhœa persists as a serious public-health hazard.

A group of diseases partly old and previous unrecognised, and perhaps partly new or more virulent, is those caused by viruses. Besides such well-known viruses as those of poliomyelitis, influenza, and trachoma, a whole host of new agents has been found in Africa. Much of this research has been done in the South African Poliomyelitis Foundation supported by a team from the Rockefeller Foundation.

Two examples of conditions aggravated by the stresses in a society shifting from the pastoral to the modern are tuberculosis and industrial disease. Unfortunately tuberculosis is increasing in nearly all African territories, especially in the town and labouring groups. The story of industrial expansion in other continents is unhappily repeated. Again, increasingly as the New Africa becomes industrialised, the problems of disease in mines and factories will arise, especially if the vigilance of the national health and labour administrations slackens.

Modern life is not only putting people into factories and towns; it is altering the agricultural scene. More and more large-scale agriculture in Africa is dependent upon irrigation. This is spreading bilharziasis and making the control of its snail vector more difficult. Several other parasitic worm diseases and intestinal infections continue to cause much sickness and inefficiency throughout tropical areas. Their reduction must await improved sanitary services and higher personal standards of cleanliness.

In the new pattern of disease one feature is becoming more and more striking—accidents. Even in remote regions of Africa accidental injuries are serious. Every new road brings an almost incredible number of car and lorry fatalities and cripplings. In New Africa, as in the rest of the world, the accident of the home, road, and factory is killing and maiming people and filling hospitals in ever larger numbers.

As the acute diseases recede and as the chance of living longer in a modern world increases, the so-called chronic degenerative conditions obtrude themselves. Here, too, Africa shows signs of copying the world design. Whatever may be the full story of their causes and associations the melancholy record in more and more countries is of death and disability from heart and kidney disease, nerve degenerations, and malignant disease. The mental afflictions, too, will probably be more obvious in the future Africa.

WHAT PATTERN FOR MEDICINE?

The speed and confusion of events are unfavourable to prophecy, but once the transition to sovereignity is achieved and a new African political condition is created, what will be the philosophy and form of its medicine?

In an immediate technical sense there will be enormous tasks to shoulder. The prospects of rewarding careers will lie before the new African doctors and nurses—suffering to be relieved, premature mortality to be challenged, fuller and healthier lives to be sought for the growing millions. They will also have an enviable opportunity to probe many remaining mysteries in disease. They will be the privileged observers of the whole gigantic phenomenon of a people being changed by social pressure to accept new ways of life. Such tantalising questions as the effects of climate and environment on energy, mental capacity, physiological efficiency will be theirs to study. Medicine in the New Africa will be rich in obligation and in opportunity for research.

Public-health and preventive medical measures to meet the challenge will only be effective, indeed possible, if the general administration is competent. But even assuming that no disastrous weakness appears in the public-health organisations of the New Africa, its future medical philosophy is still uncertain.

Medicine at its best is something finer than an exercise of technical skill. In the medicine being introduced into Africa and other developing regions this broader duty is too often neglected. Yet here the need is more desperate than in the older lands where all upbringing supports understanding of such social responsibilities. The culture and civilisation which have produced modern medicine, and of which it can be a noble component, are also essential in the new countries if they are to gain completely. Medicine's true teachers and disciples give more to Africa than medical care in a hospital or clinic. Their integrity and philosophy are a demonstration of the goodness to be found in their culture. This is necessary if the struggling new African medicine is to be something more than a mere materialistic technique or rival to tribal witchcraft, which could easily revive under a cloak of African nationalism.

Western medicine in helping Africa should not overlook the need for this broader interpretation of its possible service. It should guide Africa to create people who are good doctors and nurses, but are also prepared to follow fearlessly the principles founded over many difficult generations in Europe and America. This responsibility will be more onerous in New Africa than in the older settled communities of Europe and America. But the future African doctor, by being a man of integrity and principle, will increase the stability of his country and the respect it will earn in the world.

Special Articles

THE MINISTER ON THE HEALTH SERVICE

Mr. Enoch Powell, Minister of Health, reviewed the structure of the National Health Service in an address to a joint meeting of the English and Welsh Executive Councils Associations at Llandudno on Oct. 27. He said:

"The National Health Service, by its very nature as a comprehensive State service, holds out dangers and possibilities of harm as well as opportunities and possibilities for good. We can never wholly eliminate the risks and be left with only the opportunities. What we have to do is to discern as clearly as possible where those risks lurk and what they are. We shall then be in the best position to counteract and minimise them."

The service was the channel through which flowed the overwhelmingly large proportion of our national income which we devoted to the care of health and the treatment of the sick. The fraction so devoted had not, on average, been much larger during the last decade than it was twenty years earlier—though, of course, the national income itself had been larger and so, consequently, had been the absolute amount of resources devoted to medical care. One thing was certain: as our national income continued to rise, the volume of effort and resources devoted to health would rise. Another thing, too, was certain—that with the inevitable changes in the texture of society and in the content of medical knowledge and theory, the nature of the resources and the application of the effort devoted to health would also alter. In any given state of society and medical knowledge there was an ideal application of the available resources which would yield the greatest harvest in terms of health, wellbeing, comfort, reassurance—in short, of happiness. We should never quite attain this ideal, but we ought always to be tending towards it, and success or failure in doing so depended on the nature and the functioning of the channels through which the available resources flowed. Mr. Powell continued:

"It is in this context that a comprehensive State service has its dangers. In such a service responsibility is inevitably centralised—in the Minister answerable in Parliament. Because responsibility is centralised, so, in large measure, must be decision, since responsibility implies the power to take the decisions for which one is answerable. This in turn implies an administrative machine which will link all the parts together and secure conformity with the central policy and decisions. Now, all this brings with it a great danger—that of rigidity. Policies which are formed centrally and executed administratively are bound to be slower to change and less adaptable to alterations of circumstance and demand than if responsibility were diffused and decisions were independent. The great machine is bound to have a one-track mind, to be cumbrous and unresponsive, to abhor variations, to be insensitive to the world around it.

"These disadvantages apply anywhere; but in the field of health and medical care they can be specially dangerous. Here is a field in which it is the individual mind, the local experiment, even the chance observation, which bring about the great advances. The man or woman who is (as we say) before

his time, at whom officialdom is bound to look askance, whom contemporaries treat as an oddity or a nuisance, turns out to be the pioneer, doing the work which determines the direction of future development. These people need an environment in which they have opportunity, even encouragement, certainly not repression. But how is the machine to know them when it sees them?"

Not only the methods of giving medical care, but the character of the need for it were constantly changing. Post-war legislation and planning for all the welfare services reflected the conditions of the pre-war world: for it had nothing else to go on. They were trying now to assess the revolution of the 1950s; but it might be far into the 1970s before they could adjust the machinery to take account of it. This conflict between the characteristics of a comprehensive State service and the facts of social change and medical progress could never be fully resolved; for it was inherent. But by recognising it, there was much they could do to limit and counteract its dangers.

Those who framed and hammered out the National Health Service were not unconscious of the dangers, and they deliberately embodied in its structure elements of independence, both lay and professional, to be a counterpoise. The contractual status of the general practitioners, dentists, and opticians, the separate representation of the doctors and other professions in the structure of the hospital and executive council services, the power and authority of the professional colleges and associations—these might seem to have a fine old English illogicality in a State service. "But a wise Minister of Health will see in them not hindrances but safeguards to the soundness of his work, and in all that I do or seek to do I shall be as jealous of the independence of the professions as they are themselves," said Mr. Powell.

But all these built-in counterpoises in the structure of the National Health Service to the dangers of the great machine would not be sufficient if the great machine itself were all. "The National Health Service is intended to be comprehensive; it is not in my view intended to be exclusive," went on Mr. Powell. "For the service's own sake, I attach the highest value to the fact that medical service and care is also available outside it and that completely independent organisations exist in the field, to support and conduct research, to study and criticise, to supplement, assist, and (why not?) overlap the services provided by authority of Parliament." He welcomed the flexibility and spontaneity which these other channels bring to the nation's provision for health.

Mr. Powell recognised three trends in the modern approach to health and medical care: (1) the growth of community care and aftercare of the sick, "which takes off the hospitals work which can be done more effectively and more beneficially outside them"; (2) the development of preventive and remedial measures which will prevent admission to hospital or lengthy treatment there; and (3) the more intensive and efficient use of hospital accommodation, expressing itself in higher turnover of patients and lower ratio of beds to population. In two of these three the initiative in development lay with the local authorities; and if the new trends were to find full expression, the biggest expansion within the health service in the next decade would have to come on the side of local government. One should note finally that as the link between the three trends is, from one point of view, the patient as an individual human being, so the link from another point of view is the friend and adviser of the patient as an individual human being—namely, the general practitioner.

Turning to finance, Mr. Powell declared that the financial structure of the National Health Service could not have been devised more effectually if the object had been to put the three main elements into watertight, non-communicating compartments. There were in fact three separate financial systems, and consequently the interrelation between developments and decisions in each of the three fields was virtually impossible to express in the clear financial terms which would so much help administration and public understanding. "However, I must say bluntly that a major reform in the financial structure of the National Health Service is farther off at present than the eye of a politician can see. . . . We must work with the structure we have got, and I shall not be content until I can see a long-term picture in which the development of the hospital service is dovetailed with the development of the local-authority services, and the future function of the family practitioner is related to both."

Dialogues of Today

SOCRATES, THIS IS YOUR LIFE!

HAEMON: Come in, Socrates, and don't be surprised to see so many people. We know that you are becoming an author yourself for the first time, so we thought we would like to congratulate you. Socrates, this is your life!

SOCRATES: It is true, Haemon, that I am no longer to be dependent upon Plato and Xenophon for an account of my words, but I am no author: any ideas to be found in my conversations are contributed by those with whom I talk. I am only a midwife, delivering other people of their ideas.

HAEMON: Come in, Apollodorus, and tell us how you first met Socrates.

SOCRATES: Welcome Apollodorus! What have you been doing today?

APOLLODORUS: I have been in court arguing as to whether or not certain words are obscene.

SOCRATES: Is there any more important question?

APOLLODORUS: I should hardly have called it important, Socrates.

SOCRATES: But tell me, is not obscenity sometimes a kind of swearing?

APOLLODORUS: Sometimes it is.

SOCRATES: And when men swear do they not use words, which are held sacred, in a way which is considered blasphemous?

APOLLODORUS: Certainly.

SOCRATES: It would seem then that if we are to decide why words are obscene we must also consider what makes words sacred, and we can hardly do that without asking what is sacred, and why it is so. So you see why I said that the nature of obscenity is a most important question. But, tell me, is there any characteristic of the obscene words themselves which distinguishes them from other words?

APOLLODORUS: I don't know of any.

SOCRATES: Are they not all short words, usually of one syllable?

APOLLODORUS: I suppose that is true, but surely it is not the form of the word but the meaning which renders it obscene.

SOCRATES: Surely not, Apollodorus, for if instead of a word of four letters you use an equivalent one of four syllables, the feelings of your hearer will be quite different, although the

meaning is the same. Does it not seem to you that a short word contains all its energy in a small space and at high tension, and at once conveys to us a physical reality, whereas a word of four syllables carries its energy at low tension, and so conveys a meaning which is emotionally diluted, and makes far less impression on the feelings?

HAEMON: Thank you, Apollodorus! Now here is Analyticus.

SOCRATES: It is appropriate that you should have come just now, Analyticus, when we are talking about obscenity, for are there not many people who think all your writings obscene, even though you use many words of more than four syllables?

ANALYTICUS: Yes, indeed, Socrates, but when I am called a corrupter of youth I console myself with the fact that they call you the same.

SOCRATES: Tell us why you think some words are obscene.

ANALYTICUS: I think the form of the word is only one factor, important though it is. A word may transmit emotion forcibly, but the emotion is related to the thing signified. If some things were not sacred swearing would lose its point, but so it would if it were not considered reprehensible, and it is reprehensible only because some things are sacred. People sometimes speak of obscenity as animalism, but that is just what it is not. Animals alone are innocent of obscenity. Obscenity implies a sense of guilt. If you never swear you are either perfectly balanced or too conscious of your own guilt.

HAEMON: Here is Eryximachus.

SOCRATES: Welcome, Eryximachus, for there is no one more fitted than you to explain to us the nature of obscenity, since no one behaves more shamelessly than you.

ERYXIMACHUS: How is that, Socrates?

SOCRATES: Do you not discuss with your patients matters which they would be ashamed to talk about with anyone but a doctor, and when you examine them do you not insist that they should conceal nothing which their modesty makes them conceal from others? And in all this do either you or your patients feel any shame?

ERYXIMACHUS: But there is nothing obscene in all that, Socrates, for modesty is a matter of convention and shame does not arise in the relation between doctor and patient.

SOCRATES: It is the same with me, for I am not only a midwife who delivers men of their ideas, I am also a physician who seeks to examine their thoughts in all their nakedness and a surgeon who practises the orthopædics of the mind. And it is my aim to examine men's words and to persuade them to let them be examined in the same spirit of truth with which Eryximachus examines their bodies.

HAEMON: I am sure we all wish your book the success it deserves. Socrates, master of words, this is . . .

XANTHIPPE (*marching firmly into the room*): . . . your wife! I'll give you words! Was there ever such a man? He hasn't slept for two nights, yet here he is talking about words. And he drinks twice as much as anyone else without getting drunk, and sleeps out of doors wherever he finds himself, without even a blanket. But what does any of you care so long as you can get him to discuss philosophy? I'll give you a bit of philosophy. Where do his words come from? Where does his life come from? Ultimately from my kitchen. Think that one out, all of you! Come on, Socrates, we're going home.

(*They go.*)

The Widdicombe File

LXVI.—THE DIVISION OF PATHOLOGISTS

DEAR PETER,

I thought your letter* was a very sound and moderate statement of the case—as stated by a supporter of a Faculty with the Physicians. Of course you were trying to be impartial, just as every decent pathologist tries to be when he rehearses the arguments, but it is just impossible. The only man who can be truly impartial is the man who does not care one way or the other, and he will not trouble to rehearse the arguments at all. That presidential address which you rightly describe as statesmanlike was, I know, meant to be impartial; but to me the final section seems to emphasise the advantages of a Faculty and the disadvantages of a College.

You have recited some of the arguments for and against both sides, and I would like to review some of them as a supporter of the College. You quote the argument that the establishment of a College "would be a cripplingly expensive undertaking", but this is obviously untrue unless we develop delusions of grandeur and try to obtain in a few years the sort of accommodation which other colleges have taken centuries to build up. The independent Faculty of Radiologists, which is doing for radiology what a College would be trying to do for pathology in its early years, is able to exist simply and economically, and so could we. You quote the argument that any examination set up by the College would take many years to achieve recognition, but what is the evidence to support this view? There is after all no really satisfactory examination at present for would-be consultant clinical pathologists, and if a College of Pathologists provides a good one I can see no reason why it should not quickly become accepted.

As for the College of Physicians, it is difficult to consider it as anything but what the name implies, even though I agree that it is not exclusive, and accept that out of every 100 "active Fellows" there are about 11 administrators, 9 pathologists, 6 academic pharmacologists, physiologists, or research-workers, 2 radiologists, and an obstetrician. It could, of course, cease to be primarily a physician's college, but is that the wish of most physicians? I would agree that most clinical pathologists, if they had taken up any other specialty, would probably have wished to become physicians rather than surgeons or obstetricians. But clinical pathologists are still not physicians except in so far as a few hæmatologists have their own patients, and although we certainly must remain *clinical* I see no reason why we should enter into closer relations with the physicians than with any other special group of doctors.

"If we were all certain that we could trust the Physicians", you say, "I think few would hesitate to accept their offer". I think you miss the point. This is not a matter of trust, but a matter of intelligent anticipation of the possibility that the interests of physicians may not always coincide with those of pathologists. If they do, well and good; but suppose they do not? You say that "if, after an honest trial . . . we found ourselves unable to agree with them, nothing could stop the faculty then splitting off". I think you overlook the fact that the Faculty would be a creation of the College of Physicians, not of pathologists, and it could hardly split off as a body unless the parent college chose to abolish the Faculty. Are you prepared to envisage a future situation when a body of dissatisfied pathologists has to try to set up an independent college in opposition to an established

* We printed this letter from the File on Oct. 22.—ED. L.

faculty? Then indeed the " dissensions and bankruptcy " of which you warn us might well become a reality.

Our seniors often tell us that there is no advantage to them from either course, and that they are only concerned to provide for the younger pathologists in whose hands the future lies. At the same time they tend, perhaps, to ignore the experience of most of those who discuss such matters with these younger pathologists, and find that they are mostly in favour of a College. The young men do not seem to be afraid of starting in a small way provided that they can feel genuinely independent and not a sort of appendage to another college. Their " image " of pathology is of a subject which is of real importance in its own right and which can therefore expect its own separate and individual organisation.

If we are to build surely for the future, independence is the only safe choice. When I have reached retiring age, I do not want my juniors to be able to say to me: " You and your colleagues made a fine mess of things in 1960. Here we are stuck in the College of Physicians where we are not really happy, but it will be very difficult to break away now. If you had only made the effort to form a College it would be well established by now. Did you *have* to choose the easy way? Couldn't you see just a little way in front of your noses?".

Yours,

G. G.

Symposium

TICK-BORNE ENCEPHALITIS VIRUSES

FROM A CORRESPONDENT

THE Institute of Virology of the Czechoslovak Academy of Sciences acted as hosts to virologists from eleven different countries during a four-day symposium last month on the biology of viruses of the tick-borne encephalitis complex. The meetings were held in delightful surroundings at the House of Scientists at Smolenice, near Bratislava. Representatives from almost all the major groups working on this subject were present, and the symposium provided an unusual opportunity for workers from many different disciplines to pool information and exchange ideas in a common approach. In Britain, human infections with louping-ill virus do not present a serious public-health problem; but in Central Europe, Scandinavia, U.S.S.R., and India viruses of the tick-borne encephalitis group are a serious menace. The recent recognition of human infections with viruses of this group in Canada [1 2] and the U.S.A. [3] extends the area in which these viruses are known.

Dr. J. CASALS (New York) showed how the tick-borne viruses were placed with yellow fever and some twenty other arthropod-borne viruses into the serological group B on the basis of antigenic relationships. In the past, the tick-borne encephalitis viruses have been considered a homogeneous group in spite of wide differences in the disease patterns they produced in different parts of the world. Dr. D. H. CLARKE (New York) showed that they could be divided into six antigenic sub-groups on the basis of hæmagglutination inhibition tests with absorbed sera and by agar-gel precipitin tests. The six sub-groups were represented by the classical far-eastern Russian spring-summer encephalitis (R.S.S.E.), louping ill, Omsk hæmorrhagic fever, Kyasanur Forest disease,[4] Malayan tick-borne Langat virus, and Central European tick-borne encephalitis which included Czechoslovakian, Austrian, Finnish, Polish, Swedish, and Yugoslavian strains, as well as strains from European U.S.S.R. The recently described North American Powassan virus had not yet been examined by these techniques. These antigenic differences were important because they explained the reported failure of R.S.S.E. vaccine to protect humans (Dr. P. N. BHATT, Poona) or mice (Dr. L. DANEŠ, Prague) against infection with the virus of Kyasanur Forest disease.

As in other branches of virology, tissue-culture techniques were gradually replacing older methods for the titration of viruses and for the detection of neutralising antibodies. The use of a plaque technique for the titration of tick-borne encephalitis viruses was described by Dr. J. S. PORTERFIELD (London) and was applied by Dr. V. MAYER, Dr. J. ZAVADÁ, and Dr. R. ŠKODA (Bratislava) to Central European strains. Dr. BHATT reported that chick fibroblast cultures were as satisfactory as mice for the primary isolation of Kyasanur Forest disease virus. Czechoslovak workers preferred a two-stage process—primary isolation in tissue-culture cells which were later shown to be infected by virtue of their resistance to a challenge virus. Neutralising antibodies were detected by a metabolic inhibition test carried out in Hela cells (Dr. H. LÍBIKOVÁ and Dr. J. VILČEK, Bratislava), by plaque inhibition (Dr. J. S. PORTERFIELD, London), or by the direct inhibition of cytopathic effect in Hela cells (Dr. E. MOLNAR, Budapest) or in pig kidney cells (Dr. D. MÁLKOVÁ, Dr. Z. MARHOUL, Dr. V. FRAŇKOVÁ, and Dr. V. ČERNÝ, Prague).

Vaccines derived from formalinised mouse brain had been used for many years in the U.S.S.R. (Prof. E. N. LEVKOVICH, Moscow, Prof. A. A. SMORODINSTEV, and Dr. V. I. ILYENKO, Leningrad) and formalin-inactivated louping-ill vaccine had been used to protect laboratory personnel (Dr. D. G. FF. EDWARD, Beckenham) and domestic animals (Dr. D. BLAŠCOVIČ and others, Bratislava). Attempts at producing a vaccine from virus grown in tissue culture were reported from Prague (Dr. R. BENDA and Dr. DANES), from Budapest (Dr. E. MOLNAR), and from the U.S.S.R. The major difficulty was to guarantee complete destruction of infectivity without at the same time reducing the antigenicity of the vaccine. There were many parallels with the poliomyelitis vaccine problems. A further important factor reported by Dr. G. D. ZASUKHINA (Moscow) was that virus grown in tissue culture with a deficient medium was less antigenic than virus grown in a rich medium.

The maintenance of the tick-borne viruses in Nature is still not completely understood. The course of infection in an experimental animal, the laboratory mouse, was studied by Dr. P. ALBRECHT (Bratislava) in an elegant series of experiments based on the use of fluorescent antibody techniques. Other animals which may be infected in Nature include bats and lizards (Dr. J. REHÁČEK, Dr. J. NOSEK, and Dr. M. GREŠIKOVÁ, Bratislava), domestic ducks (Dr. E. ERNEK, Bratislava), and coots (Prof. H. A. E. VAN TONGEREN, Leiden). Much remains to be learned about the natural history of this group of viruses. Although the great majority of infections are transmitted by the bites of infected ticks, mechanical transmission by mosquitoes (Dr. Z. ZOTOWSKI and Dr. Z. WROBLEWSKA-MULARCZYKOWA, Warsaw) or fleas (Dr. K. HEYBERGER, Dr. A. SMETANA, and Dr. B. ROSICKÝ, Prague) may play some small part in the local spread of infection, and infection by the ingestion of milk from infected goats, sheep, and cattle is now well established. The many factors which influence the natural history of viruses of the tick-borne encephalitis complex were ably reviewed by Dr. T. H. WORK (New York).

The full proceedings of the symposium will be published by the printing house of the Czechoslovak Academy of Sciences and this volume will be an authoritative summary of all present knowledge of this important group of viruses. The organisers are to be congratulated on calling together the participants and drawing forth such a full and lively exchange of ideas.

1. McClean, D. M., Donaghue, W. L. *Canad. med. Ass. J.* 1959, **80**, 708.
2. Casals, J. *ibid.* 1960, **82**, 355.
3. Thomas, L. A., Kennedy, R.C., Eklund, C. M. *Proc. Soc. exp. Biol., N.Y.* 1960, **104**, 355.

4. See *Lancet*, Oct. 29, 1960, p. 988.

In England Now

A Running Commentary by Peripatetic Correspondents

ATHEROSCLEROSIS among senior consultants is to be expected and, within reasonable limits, is perhaps right and proper. But when it strikes among your contemporaries—chaps you were at school with—complacency is shattered. So I bought a bicycle, for has it not been clearly shown by the work of whoever it was that exercise and coronaries were negatively correlated? Admittedly the idea was not entirely my own. Not long ago I chanced on a visiting physician of some eminence, washing himself down in the hospital cloakroom. He explained that he had just pedalled over from Fulham, a good fourteen miles away.

Choice of velocipede was easier than I expected, for there was only one secondhand machine of my size, and when the handlebars had been changed (the old ones scraped the ground) I was left with a good bargain. My early experience was salutary: 14 years of motoring had involved different (if any) muscles and the saddle impinged on areas of my big-end which I had long forgotten. Life on the roads as a glorified pedestrian seemed very different from the world of motorists, and it was most unnatural to have to stop at red lights. But I persevered and rode daily to and from hospital. As my reflexes, quadriceps, and some callosities developed appropriately, travelling suddenly became much more interesting. Territory I had motored over a thousand times yielded unnoticed gems of architecture or nuances of gradient. The prevailing wind started to play a part in my life. I turned again to Nature and the basic things of life without which a man's spiritual development cannot take place—such as irritable little dogs, midges, and rain down the back of your neck. Also you get a closer look at blondes in the bus queue. Even securing the aid of a bicycle shop was a new experience; no garage has charged me as little as 2*s.* for anything.

Yes, cycling has reopened a dimension in my life. Surprising what a few miles a day will do. My weight is down, muscles are up, wind is longer, mind clearer, and waist more waisted. It has been a wonderful week to recall, as I drive to my hospital with the heater on, listening to the radio.

* * *

The Comet journey to New York was a revelation in quietness, and in the extraordinary deep blue of the sky at 40,000 ft.

Lima to La Paz was more spectacular than I had imagined. After 500 miles of Peruvian desert, with the snowcapped Andes visible from 100 miles away, we went 200 miles east at 18,000 ft., just clearing the pass between the peaks. The main impression is the extraordinary colour. Over Peru it was an orange brown, with the river beds looking like skeletons of leaves pressed in grandmother's book. Then came a range of colours like those seen near the waste heaps of a chemical works, with greens and blues and greys and yellows. But since there is the largest deposit of minerals in the world here, perhaps it is no wonder. The magnitude of the scenery surpasses anything I saw in Tibet, though perhaps that's not quite fair since I've travelled more here. But in an hour or so we went by jeep past snow-covered llamas in the frosty morning, down a series of hair-pin bends dug out of a mountainside at 10° to the vertical at times, until we came to a deep valley with bananas and apples and oranges growing. Every half mile or so there are little crosses to mark a too enthusiastic driver, because there are no walls or edges to the road.

* * *

The practice of medicine in a foreign country is full of unexpected little quandaries and hazards. It's a commonplace that one's knowledge of anatomy dwindles rapidly from the day of passing the M.B., but it's not until you have to ask someone in a detailed way about their symptoms in a foreign language that you fully realise how many parts the body has. And different languages imply, so often, different points of view; for instance, we are taught in school that *s'asseoir* means *to sit down*; yet if your patient is lying flat and you want him to sit up you say *asseyez-vous*. Again, the French do not make quite the same distinction in their language as we do in ours between pain and grief; *douleur* means both. Somewhere since Malory wrote about the dolorous wounds of Arthur's knights, we have apparently forgotten that grief may be the real trouble underlying a patient's complaints of pain. Perhaps the trickiest problem one encounters in examining a patient abroad is that of vocal fremitus in the chest. Each of us solves this in his own way and one musn't be too rigid about it all. It would perhaps be a mistake to carry too far the customs of the Old Country into Basutoland where, I'm told, the word for 99 is Machoumearobilengmonoolemongametsoarobilengmonoolemong.

* * *

Reading the remarks of my colleague, lately of Lambeth, about the neighbours who persisted in addressing him as "Mister", I wondered whether he invariably refers to himself as "Doctor". Outside working hours I reserve it for certain well-defined occasions. One of these is when making appointments at the hairdressers. There by suggesting that I am terribly busy and liable to be called away at any moment, it facilitates excuses for missed appointments and enables me to get a quick shampoo and set at short notice. Again, I always use the title when I am asked to sign my name and address on the back of cheques; under these circumstances any extra evidence of respectability is of great help.

Lately it saved me from a good deal of inconvenience. My scooter was stolen from a part of London many miles from where I live. Late the same evening, the police rang to say that they had found it, and would I come to the station at once to collect it and sign the charge-sheet. Grateful but weary, I said that I would be there as soon as possible in view of the distance and the hour. "You wait there, Doctor, and we'll send a car," the station officer assured me, doubtless with the idea that at any moment I might be called upon to save a life; and the car duly arrived.

There are times, of course, when I deliberately avoid the title, but my landlady disapproves strongly of any attempts at dissimulation. If people ask for me on the phone as "Miss . . ." or use my Christian name, I hear her answer sternly, "I'll see if The Doctor is in."

* * *

Comparative textual criticism can be fun. Study of Baedeker's post-war (1958) guide to Austria and the 1929 edition provides a revealing gombarison—sorry, comparison. Though the familiar red cover with gold lettering is retained, it is no longer teutonically tubby but svelte. It contains 294 pages compared to 518, 100 of which were devoted to "Budapest, Prague and the north Bohemian spas", now omitted. (Though Hungary and Czechoslovakia had been independent countries for ten years, one would hardly gather it from the 1929 edition.) The present edition, now called an autoguide, is streamlined in other ways besides format: for instance, we no longer have blow-by-blow accounts of museums and picture-galleries with exhibits thought worthy of notice by Herr Karl mentioned in each room. There is less ancient history and esoteric information: thus we are no longer told that the Dragon Fountain or Lindwurmbrunnen in Klagenfurt is made of "chorite schist" but I was glad to see that the tablet commemorating Emanuel Hermann (1839–1902), "who invented the postcard", is still mentioned. Nor are there detailed tours of each town, starting from the railway station, but much clearer plans with "sight-seeing tours" and "through routes". In fact, modern travel is clearly no longer designed either to broaden the mind or flatten the feet. But nostalgia is catered for by the occasional survival of some of the classical phrases such as "Gasthof Lukashof, plain but well spoken of", still recalling one's aunt or members of the Women's Institute.

* * *

O, my Luve's like a red, red rose.
I hope it's nothing catching.

Letters to the Editor

FUTURE ORGANISATION OF PATHOLOGISTS

SIR,—A voting paper is about to be circulated to pathologists asking them to record their opinion for or against a division of pathology within the Royal College of Physicians, or a new College of Pathology.

We have for many years been concerned with research in pathology and with the training of pathologists, and believe that a higher examination based on a background of suitable training is essential to ensure that candidates either for hospital or academic appointments have acquired a reasonable grounding in their subject.

We both write as past presidents of the Association of Clinical Pathologists, who have been openly critical of the procrastination of the Royal College, but who are satisfied that the suggestions now put forward by it are what is required. Undoubtedly, the Royal College has been unduly tardy in making any suggestions, but the present generous and unequivocal terms make amends.

It is generally agreed that in modern conditions the membership is an unsuitable examination for pathologists. In the time available the techniques of clinical examination and of pathology cannot both be mastered.

We welcome the opportunity of still closer cooperation with our clinical colleagues. Not only are they progressively more dependent on us for confirmation of diagnosis, or indeed in many cases for provision of all the important data, but, reciprocally, we also are dependent on their acumen and powers of selection for our daily interests.

We have long believed that what is needed is:

(1) A higher qualification of the same status as the M.R.C.P. and F.R.C.S.

(2) An academic centre which would uphold the standards of pathology and help in maintaining good standards of training in pathologists.

(3) A body to speak for pathologists.

In our opinion the suggestion of the Royal College satisfies these requirements. We believe that unless this opportunity is accepted there will be a very long delay before we realise our ambitions.

JOAN TAYLOR
R. J. V. PULVERTAFT.

London.

SIR,—Much has been said and written on this subject by the more learned and senior practitioners of our specialty, but little by the juniors. As one of their number may I put forward three points.

The primary reason for any alteration in the present position is to ensure recognition of the status of pathologists, despite the fact that a man's status depends above all upon his personality and the quality of his work, and only secondarily upon his qualifications. Higher qualifications, however, are necessary to prove adequate training in one's own specialty for promotion to consultant or similar grade, and the institution of a specialist examination in pathology, of the highest standard, is now urgently required. To the pathologist in training it is the most important facet of the present discussions. The expenditure of time and work by those who aspire to the membership of one of the Royal Colleges of Physicians has been eloquently described by Professor Cappell in his presidential address [1] to the Association of Clinical Pathologists. It is certain that only the qualification offered by the Royal College of Physicians will have the immediate high standing required to divert them from such examinations.

The finances of the new organisation are of particular interest to impecunious registrars and lecturers. It has been said that the provision and maintenance of any reasonable building will cost each member an initial donation of about £100 and an annual subscription of up to £25! Some of us may not be able to find such a sum. Are we to be excluded from the college until we are senior enough to afford the subscription, and if so will we ever achieve the seniority? However, we are assured that industry and various benevolent foundations will provide the necessary funds. Even if the money is forthcoming, I do not believe we can justify spending such vast sums on establishing a college, when there are so many research projects urgently needing finance. Would our money not be better spent on research on acute leukæmia in children or even coronary disease in pathologists than upon a building? £100,000 would buy a lot of knowledge of disease—could we not devote our benefactions (if any) to establishing a series of research fellowships rather than a college?

If a College of Pathology is to be founded then I believe it must be as broadly based as possible and must be open freely to all those who work in and around the subject, scientist or doctor, whether academic or clinical. Pathology is neither practised nor advanced solely by those on the Medical Register. However, in a Faculty of the Royal College of Physicians it would be logical to restrict full membership to the medically qualified.

The College of Physicians of London is a body of the highest standing and to be called a physician is no dishonour. I hope, with Peter Davey,[2] that a Faculty will be established. They offer us more than does an independent college in the foreseeable future, and at less cost. The generosity of their terms puts us in an immensely strong position, and we can always withdraw.

Finally, may I suggest abandonment of the term "Division of Pathology", for the words come uncomfortably close to the truth.

London, S.W.15. P. O'GORMAN.

*** Another view on this subject is given on p. 1025 in a letter from the Widdicombe File.—ED. L.

ATHEROSCLEROSIS AND CORONARY HEART-DISEASE

SIR,—Surely your correspondents are arguing on points of semantics rather than pathology. As you, Sir, rightly pointed out last year,[3] patients do not suffer or die from coronary disease, but from the consequences of myocardial ischæmia, which may be acute, chronic, or spasmodic. I have always held that one of the best classifications of disease causation, is that which we learned at our obstetrician's knee, of which a part ran—faults in the powers, faults in the passages, faults in the passenger. Myocardial ischæmia may be due to faults in the power of the heart's action, faults in the coronary passages whether narrowed or occluded by what you will, or faults in the passenger—the blood, which may be deficient in oxygen-carrying capacity, or contain a substance noxious to the myocardium.

In spite of the welter of investigations on atheroma and degenerative heart-disease, we remain remarkably ignorant as to the frequency, degree, and type of myocardial ischæmic change to be found at death in the population

1. *Lancet*, Oct. 15, 1960, p. 863.

2. See *ibid.* Oct. 22, 1960, p. 921.
3. *Lancet*, 1959, ii, 863.

as a whole, and without this many of our deductions in this field are insecure. I believe that a study, almost completed here by Dr. C. J. Schwartz and Dr. J. R. A. Mitchell, will give us this information, as far as the current Oxford postmortem population is concerned, and may encourage others to carry out comparable investigations elsewhere.

No-one would dispute that one may find coronary narrowing or occlusion in hearts from persons of all ages, yet it remains that in a high proportion of elderly persons, ischæmic myocardial lesions occur, which are quite different in character from those usually seen in the younger age-groups; for example, there is the condition which Linzbach called reticular myocardial necrosis, but unhappily this is a sphere of cardiac pathology which to a large extent is unexplored.

Turning to the Registrar-General's statistics, we find some curious features:

England and Wales: Crude Death-rate to a million living

	1940	*1949*	*1958*
Arteriosclerotic heart-disease, including coronary disease (I.S.C. 420)	573	1093	1863
Myocardial degeneration with arteriosclerosis (I.S.C. 442.1)	467	617	532
Other myocardial degeneration (I.S.C. 422.2) ..	1548	1274	656
Total degenerative heart-disease (I.S.C. 420 + 442.1/2	2588	2984	3051

As everyone knows, the death-rate attributed to "arteriosclerotic heart-disease and coronary disease" has increased more than threefold in the past eighteen years, but "myocardial degeneration with arteriosclerosis" has hardly changed at all and "other myocardial degeneration" has fallen to a third, so that if one groups together the rubrics that can be regarded as representing ischæmic heart-disease (I.S.C. 420, 422.1, 422.2), the rate has only increased by a fifth, which is little more than is to be anticipated in view of the increased expectation of life. I am, of course, as aware of the defects of comparison of crude death-rates as against standardised mortality ratios, as I am of the answer which John Graunt found to his question, why there were so few deaths attributed to the Pox in the Bills of Mortality. Nevertheless, it might be worth while, for those who believe, that by feeding rabbits or men on unnatural diets, they will determine what factors in modern life have caused this spectacular increase in deaths attributed to "coronary disease", to try and find out what are the factors which have caused the almost equally spectacular decrease in deaths attributed to "myocardial degeneration".

When we look at the age-differences, the Registrar-General's tables reveal another curious feature:

England and Wales: Age-differences

	Proportion of Deaths Over 65			*No. of Deaths: 1958*		
	1940	*1949*	*1958*	*<65 yr.*	*65+yr.*	*Total*
All causes	53%	63%	68%	..	..	..
Arteriosclerotic heart-disease, including coronary disease (I.S.C. 420) ..	55%	65%	69%	25,962	58,079	84,041
Myocardial degeneration (I.S.C. 422)	85%	90%	95%	2195	51,577	53,772

As is to be expected in an ageing population, the proportion of all deaths occurring over 65 is steadily rising; in 1940 it was 53% and in 1958 68%, and the proportions of deaths attributed to arteriosclerotic heart and coronary disease is almost identical (1940 55%; 1958 69%), but of the deaths attributed to myocardial degeneration, 85% occurred at 65 and over, in 1940 and 95% in 1958.

Putting this in another way; in 1958 there were 138,000 deaths attributed to "arteriosclerotic heart and coronary disease" and "myocardial degeneration", of which only 20% occurred under the age of 65. Of these 28,000 deaths under 65, 94% were attributed to arteriosclerotic heart and coronary disease, whereas of the 110,000 deaths over 65, 47% were attributed to myocardial degeneration.

There are clearly a number of explanations for this difference, but it must be assumed that certifying doctors consider that there is a fatal form of heart-disease which they designate as "myocardial degeneration" or any of the other inclusion terms in rubric 422, which occurs almost exclusively in persons of 65 and over, and accounts for nearly half of the cases of degenerative heart-disease in this higher age-group.

Naturally we have no idea what, if any, are the clinical differences or morbid anatomical lesions in cases attributed to these two rubrics but if there are real differences, other than the whims of nomenclature of the certifying doctors, then it would be in keeping with Dr. Acheson's [4] observations.

Department of Pathology,
Radcliffe Infirmary,
Oxford.

A. H. T. ROBB-SMITH.

SARCOIDOSIS TREATED WITH CHLOROQUINE

SIR,—I have read with interest Dr. Söderström's article of Oct. 29 in which he described the response of two patients with sarcoidosis to mepacrine. He suggested that chloroquine may be used instead of mepacrine.

I have treated with chloroquine systemic lupus erythematosus, periarteritis nodosa, Stevens-Johnson syndrome, and other hypersensitivity states since 1953 and rheumatoid arthritis since 1954.[5 6]

The ætiology of sarcoidosis is still unproven, but there is a fairly strong suggestion that hypersensitivity may again play a part. Michael [7] and Cummings,[8] for instance, related sarcoidosis to the chemical constituents of pine pollen.

On the assumption that sarcoidosis represented a hypersensitivity state I have treated two cases with chloroquine since 1957.

A married woman, aged 32, was first diagnosed as sarcoidosis, involving mainly the lungs, in 1956 when treatment was started with chloroquine sulphate 200 mg. t.d.s. This was continued for six months when it was stopped because of pregnancy. By then all lung lesions had cleared. Her condition was reviewed in 1957 and 1958, when she was quite well and the X-ray films showed clear lung fields.

A married woman of 23 was first seen in July, 1957, when she had characteristic sarcoid lesions on her upper arms, trunk, and buttocks, and hilar-gland enlargement. Biopsy confirmed the clinical diagnosis. The Mantoux test was negative. Chloroquine sulphate 200 mg. t.d.s. was started in July, 1957. In September, 1957, the hilar enlargement had greatly diminished and the skin lesions subsided. In February, 1959, she was entirely symptomless and stopped chloroquine on her own. By May, 1959, there was a recurrence of lesions on the right side of her cheek, upper arms, and buttock. Chloroquine was immediately re-started, and by July, 1960, the skin lesions had almost completely disappeared and she felt well. This patient is still on 200 mg. chloroquine sulphate daily.

At the international conference on sarcoidosis in Washington, D.C., this year several speakers described the beneficial effect of chloroquine in sarcoidosis.

Evaluation of any drug for sarcoidosis is difficult because of the fluctuation in the natural history of the disease with frequent spontaneous remissions. This was the reason for not publishing my own limited experience of the drug in sarcoidosis. If, however, since it appears that more widespread trials of chloroquine in the management of sarcoidosis are carried out in other parts of the world, then even a very limited trial such as Dr. Söderström's and my own should be made known. It is of particular interest that Dr. Söderström noted selective

4. *ibid.* 1960, ii, 706.
5. Fuld, H. *Rheumatism*, 1958, **14**, 12.
6. Fuld, H., Horwich, L. *Brit. med. J.* 1958, ii, 1199.
7. Michael, M., Jr. *Ann. intern. Med.* 1956, **45**, 151.
8. Cummings, M. M., Hudgins, P. C. *Amer. J. med. Sci.* 1958, **236**, 311.

staining of sarcoid lesions by the antimalarial. There is reason to believe that chloroquine, too, has a selective action on the joints in rheumatoid arthritis, as we have found after 18 months' experience with chloroquine injections into rheumatoid arthritic joints (details are about to be published).

Sefton General Hospital,
Liverpool. H. FULD.

HEATSTROKE

SIR,—I must congratulate you on your editorial of Oct. 15. Such is the reputation of your journal, however, that unless I take issue with you on a matter of emphasis it may appear that treatment in a special room with refrigerated water, as described by Guthrie and McCraken,[1] is the best and only satisfactory method of treatment. I know that special rooms of this nature are provided in the Persian Gulf—but many a heatstroke has been treated successfully with only the minimum of facilities. I feel that it would be better to emphasise the principles of treatment rather than the accessories, which are expensive.

At the moment there appear to be two schools of thought on treatment: one uses refrigerated water or iced baths or iced sheets and the other artificial sweat and forced air movement. I am a convert to the second school ever since I encountered shivering as a response to treatment with iced sheets in a patient who was still hyperpyrexial. After this I began to reconsider the physics of reducing body temperature.

Everyone knows that during treatment it is important not to reduce the temperature to normal limits as this may give rise to shock, and if shock occurs it is very difficult to treat. Immersion in an iced bath can be very "shocking" to even a normal individual: just jump naked into the Serpentine next January if you wish to contest this point! Immersion in, or spraying with, refrigerated water coils the body by conduction alone and is associated, sooner or later as the body cools, with peripheral vasoconstriction. This vasoconstriction converts the skin, with its superficial fat, into a fairly useful insulating layer.

Heatstroke is related to cessation of sweating however caused. Evaporation of sweat from the skin, by virtue of the latent heat necessary to effect this, rapidly cools the blood flowing through the dilated skin vessels, which then act as a heat exchanger to the internal organs. When sweating has ceased it is logical to provide artificial sweat in the form of tepid water and to aid evaporation with strong air movement. In hot climates a powerful fan and tepid water are almost universally available, and it is usually possible soon to accelerate cerebral cooling with an ice bag, or even ice wrapped in a towel, applied to the head.

I have no wish to decry the work of anyone who uses refrigerated water or iced baths, because I feel that in their experienced hands this form of treatment is both successful and safe. To the average doctor, however, heatstroke is a comparatively uncommon emergency and treatment must be given at once with facilities readily available. I can assure you that it is perfectly possible to treat successfully hyperpyrexia of any ætiology by sponging with tepid water and a strong air blast from a fan, even in conditions of high relative humidity and high ambient temperature.

R.A.F. Institute of Pathology and
Tropical Medicine,
Halton, Aylesbury, Bucks. R. MORTIMER.

SIR,—Your leader is very valuable. Hyperthermia (as we used to call it) will follow the treatment of patients with malaria, sandfly fever, enteric fever, and influenza in uncooled hospital wards. Cardiac failure is uncommon in hyperthermia, except when the condition has persisted untreated for some hours.

Servicemen have been known to report sick, with pyrexia, and been sent back to their quarters, and found hyperthermic and unconscious some hours later; in such cases cardiac failure is not uncommon and the response to the most enlightened treatment is disappointing.

As you say, proper application of the principles of prevention, which are well known, should be everywhere applied, especially in Service communities; and devices for effective cooling should be at hand in all situations where heatstroke is known to occur. I emphasised this in 1937.[1]

St. Margaret's Hospital,
Epping. FRANK MARSH.

1. Guthrie, J., McCraken, A. V. *Lancet*, 1960, i, 682.

SPONTANEOUS FRACTURE OF THE FIBULA

SIR,—Dr. Hobbs (Oct. 22) raises an interesting point when he states that in fatigue fractures of the fibula no adequate explanation of their occurrence has been given.

These fractures occur in two main groups: (1) the young and athletic and (2) the middle-aged and tired. The case described clearly is of the second type. Fatigue in bone may be compared in some respects to that in other materials such as metal. When a metal column is subjected to repeated eccentric loadings, alternating tensile and compressive strains occur and eventually lead to a fatigue or stress fracture. This also happens experimentally in bone. Gaynor Evans [2] reported on subjecting a piece of fibula to repeated cyclical loadings at 5000 lb. per square inch, and after 3,000,000 such loadings fatigue fractures occurred.

In life, however, bone has a built-in capacity to repair by osteoblastic action and only when the stimuli are repeated sufficiently within the time taken to repair is a fatigue fracture liable to occur. This period is likely to be prolonged in the middle-aged. Even then, if aching causes the activity to cease, the early fracture may pass unrecognised.

Windsor. ROY MAUDSLEY.

POLIOVIRUS-NEUTRALISING ANTIBODIES IN STOOLS

SIR,—Dr. Godtfredsen's letter of Aug. 13 reported failure to demonstrate poliovirus-neutralising antibody in the stools of 13 convalescent individuals. We appreciate being informed of these results and hope that she and others will not cease efforts to determine the nature of resistance of the human alimentary tract to poliovirus following infection with wild polioviruses or the feeding of attenuated living poliovirus vaccines. Such alimentary resistance does not accompany Salk vaccination.

Our communication [3] reported the demonstration of specific antibody in the stools of 13 children recovering from poliomyelitis. Actually this represented only the positive results; the tests were performed in 93 convalescing patients and *only* 13 individuals were positive. Once a given stool is demonstrated to contain type-specific poliovirus antibody, the observation can be repeated and appreciable loss of titre through storage and re-thawing has not been observed. The serotype of antibody observed in our 13 positive children were: 5 for type 1; 3 for type 2; 4 for type 3. One child's specimens neutralised types 1 and 2. When antibody was found in the stools the same type (and of course one or both remaining types) of antibody was found in the serum. As we pointed out, the stool antibody when found was always *heterotypic* to the infecting virus, suggesting that those individuals' alimentary tracts had had previous exposure(s) to poliovirus.

Deviations in Dr. Godtfredsen's technique from ours include our use of a suspended-cell technique, which has advantages in demonstrating "low-avidity" antibody, and our use of 0·25 ml. of the stools tested instead of 0·1 ml.

1. British Encyclopædia of Medical Practice; vol. vi, p. 396. London, 1937.
2. Gaynor Evans, F. Stress and Strain in Bone. Springfield, Ill., 1957.
3. *Lancet*, 1959, ii, 272.

Whether the test details per se are important is uncertain, but more children may need testing: our record of 13 of 93 individuals (± 14%) suggests this. Failure to demonstrate in vitro neutralising antibody of the usual kind in the stools of the remaining 80 patients may be purely technical or may have fundamental explanations. The age of patient, time of stool-collections after the current infection, previous alimentary contact with the other serotypes of poliovirus, the "secretor" status of the patient's alimentary tract, and other factors may influence the results.

Ascertaining the modus by which the alimentary tract resists infection after experience with live virus but not following intramuscular vaccination is important from the epidemiological, clinical, and general biological points of view. It is hoped that studies of this kind with varying approaches in technique will be conducted by as many workers as can interest themselves in this field.

University of Louisville, Kentucky.

ALEX J. STEIGMAN
MURRAY M. LIPTON.

STERILISATION OF THE DIABETIC'S SYRINGE

SIR,—The recent correspondence on this subject recommends several methods to be safe and trouble-free.

On the one hand, Dr. Wauchope (Sept. 10) doubted whether sterilisation was necessary and described her fortunate personal experience without any infections for many years. But I fear that many insulin patients would have less high standards of cleanliness than hers and this is a very important point not mentioned in the previous correspondence. How well I remember a young woman who, after five years of trouble-free injections, developed mysterious abscesses on both thighs. The bath she received on admission to hospital for investigation stopped all further troubles, and she told me that she had moved to a house where there was no bath and this explained her abscesses.

What do the insulin manufacturers say in their insulin packages? Nothing very definite. Most of them say that boiling in tap-water is desirable but as that is not always possible, advocate keeping the syringe and needles in spirit.

The balance of the advice given by your correspondents is to favour spirit alone, although the initiator of the correspondence, Dr. Stephen Carter, boils his syringe four times a year and uses no spirit.

London, W.1. R. D. LAWRENCE.

SUICIDE

SIR,—Reading Dr. Stewart's article of Oct. 22 it is difficult not to feel compassion for many of the 85 suicides in his series of 122 who had been suffering from various painful or disabling diseases.

Is it not time that the coroner's court formulæ, "... while the balance of his mind was disturbed" or "... while of unsound mind", should be discarded in the absence of clear evidence of mental disturbance prior to suicide? Some people who commit suicide to terminate a life that has become a life-sentence of intractable pain are taking a step that seems sensible albeit desperate.

As you report last week (p. 976), a Bill to provide that suicide and attempted suicide should no longer be criminal offences has been drawn up and approved by the Criminal Law Revision C mmittee. So need we penalise the suicide by casting an unmerited slur on his sanity just because he has committed suicide?

With regard to attempted suicide, Prof. E. Stengel [1] has for a long time taught that one of its main motivations is the appeal of a desperate individual for help from his fellow-men. Unless the family or friends of the attempted suicide are alerted to his dangerous dilemma by the suicidal attempt, the only practical step likely to prevent a second, possibly successful, attempt would seem to be bringing him before the courts and placing him on probation on condition that he receives necessary psychiatric treatment. It is to be hoped that this potentially lifesaving course will not be made more difficult if the new Bill becomes law.

London, W.1. F. R. C. CASSON.

1. *Lancet* 1952, i, 1059.

THE NATURE OF ESSENTIAL HYPERTENSION

SIR,—I really must take exception to the data which Dr. Marshall (Oct. 22) alleges add to the solution of this problem, and the conclusions he draws from these data.

My old chief, Sir Thomas Lewis, would not allow readings of blood-pressure taken by nurses to appear in scientific publications. The estimations which Dr. Marshall uses were made by "specially trained nurses at hourly intervals during one day a patient spent in hospital". They were made to the nearest even number. Dr. Marshall states that digit preference can be excluded because the nurses had no incentive. Nor had those employed by Boe, Humerfelt, and Wedervang [1] in their measurements made on 67,976 inhabitants of Bergen. Yet digit preference was more marked than in any other series I know. 85% of systolic readings (series 1) ended with 0 and only 15% with 5. For diastolic readings the percentages were 87 and 13 respectively. Diastolic pressures had a bimodal distribution in the second but not in the first sample. This bimodality was most probably due to a change in the team of nurses making the measurements. There is no analysis in Dr. Marshall's paper of the distribution of readings, nor any evidence that steps were taken to assess how accurate the readings were.

As disturbing is his statement: "Moreover, the blood-pressure figures used in this study were means of six readings taken under constant conditions." To those who work in the field of science, "constant conditions" has a clear implication, and is a state, in fact, very rarely achieved. Dr. Marshall's 134 patients "attended hospital for one day during which they rested on a bed in the supine position. Their blood-pressure was recorded hourly for six hours by specially trained nurses, who read the sphygmomanometer to the nearest even number". One could perhaps imagine that from 10 to 4 the patients lay on a bed in a side-ward and were visited only by the nurses. But this was not so. "During the one day in hospital the patients had a physical examination, chemical and microscopic examinations of the urine, estimation of the blood-urea and blood-cholesterol, an electrocardiogram, and a radiographic examination of the heart and skull."

Dr. Marshall's averages of six values, each to the nearest even number, will give him a series of integers which perhaps he might take to one place of decimals. As set out they are arranged in groups at intervals of 8 or 12 mm. Hg. He does not say how this grouping has been done. And yet it is vital to the conclusion the reader is invited to accept.

However, the worst feature of Dr. Marshall's paper is his evidence for bimodality. A protest has been made before against interpreting irregularities in frequency distribution curves as bimodality, especially when the numbers are small. Fortunately Dr. Marshall has now brought this practice to what must be the all-time low.

1. Boe, J., Humerfelt, S., Wedervang, F. *Acta med. scand.* 1957, suppl. 321.

He says: " The systolic pressures of patients over 60 years had a bimodal distribution irrespective of whether their parents died below or above the age of 65 (fig. 5)." Fig. 5 shows the frequency distribution curve of 26 patients whose parents had died under the age of 65. Here are data taken from fig. 5 for this group.

Systolic B.P.	*Frequency %*	*Actual number*
108	4	1
120	12	3
132	4	1
144	8	2
156	12	3
168	24	6
180	16	4
192	8	2
204	12	3
Total	100	25

The contention evidently is that a series 1 3 1 2 3 demonstrates bimodality.

Finally, supposing that an analysis of patients between the ages of 31 and 70 showed that there were essentially two populations as regards blood-pressure—and has this not been shown by Dr. Marshall?—could this be accepted as evidence that essential hypertension is the manifestation of a single gene? For Dr. Marshall states: " It seems likely that the appearance of a group with raised blood-pressure is caused by a hereditary factor—probably, as Platt suggested, due to a mendelian dominant." It should be clearly stated that cerebral vascular disease consists of at least three entities: occlusion of the arteries in the neck, of those within the cranium, and cerebral hæmorrhage. There is a strong suspicion that the last is more closely associated with grossly raised pressure than the first of these. Dr. Marshall says that these patients had " what was judged on clinical grounds to have been a non-embolic cerebral infarction ", but, as previously reported,[2] his trial of anticoagulant treatment had to be stopped because of the incidence of fatal cerebrovascular accidents due to cerebral hæmorrhage in the treated group. Had he indeed demonstrated two populations in cases of cerebrovascular disease this would have no bearing whatsoever on whether essential hypertension is or is not the manifestation of a single gene.

Oxford. G. W. PICKERING.

SIR,—Before some of your readers should be tempted to interpret the results found by Dr. Marshall as cogent evidence in the conflict of views on the nature of essential hypertension, could we have the answers to some simple questions?

(1) We are told that the subjects studied had all previously had what was judged to have been a non-embolic cerebral infarction. In what ways were these survivors thought to be representative of all people suffering cerebral infarction, how were the subjects selected, and why were there 91 males and only 43 females when mortality-rates from vascular lesions involving the central nervous system show no gross sex difference.

(2) Having demonstrated such very different frequency distributions of arterial pressure in the two sexes as those shown in fig. 1 (*b*) and (*c*), what is the justification for combining the two sexes in all subsequent analyses?

(3) In analysing blood-pressure data for subjects aged 31-70 is it reasonable to use only two age-groups, above and below 60, when the evidence derived from the general population shows arterial pressure to be very sensitive to age?

(4) The grouping of pressure into units of 12 mm. Hg for systolic and 8 mm. for diastolic pressure is unusual. Could this have influenced the shape of the published curves?

The type of study carried out by Dr. Marshall could be repeated in many hospitals in the country but would have little value unless confirmed in less highly selected populations. Before we are confused by more and more bimodal curves, may I make a plea, Sir, that authors should publish their data in a form that enables interested readers to evaluate them and allows comparison with other published work, and particularly with the careful work of Platt and Pickering. Pictures alone are unsatisfactory.

Llandough Hospital, Penarth, Glamorgan. W. E. MIALL.

SIR,—There seems to be a growing and unfortunate tendency, especially in communications on hypertension, to argue from diagrams. The latest example is the paper of Dr. Marshall, who relies upon them entirely and gives no figures at all. It must be admitted, however, that his sin is a minor one, for as his numbers are very small the corresponding frequencies can be reconstructed with almost complete accuracy from his curves showing percentages. Nevertheless, one would like to have the basic data in less coarsely grouped form. And, incidentally, how can pressures measured to the nearest even number be added so as to yield the series of figures shown as group centres in all the diagrams?

The following opening paragraph has appeared in chapter II in all successive editions of R. A. Fisher's *Statistical Methods for Research Workers*, right back to the first edition of thirty-five years ago:

" The preliminary examination of most data is facilitated by the use of diagrams. Diagrams prove nothing, but bring outstanding features readily to the eye; they are therefore no substitute for such critical tests as may be applied to the data, but are valuable in suggesting such tests, and in explaining the conclusions founded upon them."

The current discussion on the nature of essential hypertension will be greatly helped if these wise words are remembered, and if authors give as much of their basic data as possible, apply suitable tests, and in particular explain just what they have done, desiderata strikingly lacking in some recent papers. The curves can then serve their proper purpose of illustration and light relief.

M.R.C. Clinical Genetics Research Unit, London, W.C.1. J. A. FRASER ROBERTS.

SIR,—It has been pointed out to us that we were wrong (Oct. 15) in saying of Miall and Oldham's data[1] that there were only 24 subjects with diastolic pressures " greater than 100 mm. Hg . . . " This should have been " 105 mm. Hg and greater ", &c. We are very sorry.

S. L. MORRISON
J. N. MORRIS.

London, E.1.

CYCLICAL ŒDEMA AND SHOCK

SIR,—I read with great interest your leading article of Oct. 1. You mentioned that apparently the urine was not tested for hydroxyindole-acetic acid in the patient we described.[2]

In the interest of completeness, I should like to add that although we did not include this in the published report, the 24-hour urinary excretion of 5-hydroxyindole-acetic acid was measured on 5 occasions in this patient, including during a shock phase, during a recovery phase, and during a time when she was asymptomatic. These determinations were performed by Dr. O. Dhodanand Kowlessar at New York Hospital. The values were all between 2 and 3 mg. per 24 hours (normal up to 8 mg. per 24 hours).

New York. BAYARD CLARKSON.

2. Marshall, J. Pathogenesis and Treatment of Occlusive Arterial Disease; p. 99. London, 1960.

1. *Clin. Sci.* 1958, **17**, 409.
2. *Amer. J. med.* 1960, **29**, 193.

MODERN CLINICAL BIOCHEMISTRY

SIR,—I would not put the clock back 50 years as Dr. Hendry forbids (Oct. 29), but 113 years and quote from Virchow's paper, Standpoints in Scientific Medicine: "We can learn much from chemistry, but we will have to reserve for ourselves the privilege of applying its findings." Virchow was familiar with the appreciable number who share Dr. Hendry's outlook: in his 1855 paper on Cellular Pathology he writes: " The condescension with which the proponents of chemical and physical viewpoints—even those who have only a very imperfect understanding of microscopic anatomy—look down on morphology is well known."

From my student days I have had the highest regard for the aid we receive from competent biochemists; if they take their right place in the team they are invaluable. I strongly dislike splitting the pathology department into four or more watertight compartments. Whenever I look down my microscope problems in bacteriology, hæmatology, or biochemistry arise; with the aid of one or other member of my team these are followed to the advantage of the clinician and patient. Our biochemist regularly draws my attention to problems which should be followed in other departments. Without a medical training very few biochemists are safe in advising on the meaning of many of their findings. A good example of the interdependence of the four departments of the pathological laboratory was a man of 23 admitted to one of our surgical wards in a state of diabetic coma. When the biochemist told me of his very high blood-sugar I at once asked why he was in a surgical ward: it was because he had had a bladder-neck operation for enuresis there three months before. I discovered that he was not then a diabetic; so we at once examined his blood for severity of infection (if any), and his urine for pus and organisms. The real diagnosis was quickly established as pyonephrosis, and unfortunately proved at necropsy. To me all sections of the laboratory are equally important in general. Who is the most important departmental head varies with the case; for the young man just mentioned I would say it was the hæmatologist because he said clearly death from infection is inevitable in the absence of successful treatment.

The question of who is the most important, the pathologist or one or other of the technical heads of departments, is an absurd one. It is well answered by Leo Tolstoy in his short story Three Questions written in 1903 (in *Twenty-Three Tales*). I hope Dr. Hendry and others who think like him will read this. The practical point is that the pathologist is usually the only one who can bring all sections of the laboratory to the aid of the clinician; he above all others can cheat death when he calls too soon. The greatest emotional satisfaction is to be found in general practice, the greatest intellectual satisfaction in the pathological department. The former is warm, the latter too often cold; that is why many of us feel like Dr. Hendry at times. If this emotional satisfaction is wanted, do not become a physician or surgeon as Professor Cappell possibly suggests, for they occupy a half-way position; obtain a medical qualification and enter general practice. Dr. Hendry may be shocked to know that to me the biochemist ranks equally with the senior technician in charge of hæmatology, bacteriology, and histology. I do not know which is the most important until I know the problem. If the training of a biochemist is more difficult, and all will not agree with this, they should be paid more—as they are. This makes a psychological barrier between them and the technical heads of the other departments which a wise biochemist will do all in his power to destroy.

Biochemists are not at the crossroads looking four ways at once: at the moment they are looking on the way out only. If that happens it will be a tragedy. We do not have far to look to see non-medical biochemists who are invaluable in the practice of medicine; they are professors or of that calibre. This is taken to mean, by some, that all we need to do to obtain a good biochemical service is to appoint a good chemist in charge of it and then keep away. This is nonsense. My biochemistry department owes a lot to men with medical qualifications; these are ideal but in short supply. Even Dr. Hendry might allow that the greatest clinical biochemist of all time was the medically qualified Paul Ehrlich.

How should the pathological services of the future be planned? Division into a number of watertight compartments is an evil which may be necessary in places. The right thing seems to me a large general clinical laboratory where a problem in a patient is studied, not just a test performed. This should be backed by small reference laboratories in the same building. Most of the routine biochemistry should be done in the clinical laboratory—including the blood sugars and ureas for which Dr. Hendry has such contempt, though if I could have only two biochemical investigations I would pick these.

How should junior and senior members of the medical profession use the pathological services? I give two answers to this. Because so many tests are needed the pathologist can no longer attend to all. Many are straightforward and the patient progresses well; these cases justify a request for a given test. Many patients are diagnostic problems or are unsatisfactory. If a patient is, say, unsatisfactory after an abdominal operation I like the surgeon to tell me what he did and invite our help. At the moment many are obsessed with biochemistry to the exclusion of the other branches. The correct use of all departments will invariably say: peritonitis, ileus, both or neither. We want to know the process, not some minute detail of it. When we begin our training with the microscope we use the highest magnification we can get, and feel that if we could only obtain something larger we would know everything. As we become more experienced we use the lowest magnification so that we can see the process. This earns us scorn from the most junior: my son, when a dental student, assured me that I only guessed at such a low magnification. I fancy that many, who should know better, feel that in biochemistry they have something of higher magnification than the electron microscope. Perhaps they have; but the sap in a leaf tells you little about the plant and less about the forest.

May biochemists read Leo Tolstoy and remain our honoured colleagues. May I be permitted to salute Professor Cappell's masterly survey.

Derbyshire Royal Infirmary, Derby. G. R. OSBORN.

SIR,—There is an element of truth in Dr. Hendry's statements about the interrelationship of " pathologist " and biochemists, but surely many will think he overstates his case, and confuses any serious analysis of the position, both by his caustic wit and blatant misuse of the names of the reactants. It is patently absurd to imply that each large hospital should have an autonomous biochemistry department: such a separist movement would be harmful to the patient and the clinician, and more particularly to

the biochemist himself. What is clearly needed is a greater integration of the laboratory services, both within their own house and within the framework of the hospital as a whole. No hospital worker, be he physician, surgeon, histologist, or biochemist, can go it alone, even if the latter thinks he can do it all himself. It is, of course, platitudinous to say there is no place for the enthusiastic amateur in this modern scientific work; each specialist must overtly be trained as such, but he would be a fool indeed to suppose he alone has something to offer the patient, whatever the latter's disease.

Pathology is the study of disease: however Dr. Hendry may interpret biochemistry to himself, in clinical practice it is the application of chemistry to the study of human disease, and it must follow that even he is to some extent a pathologist. I personally would like the terms pathologist and pathology laboratory, as currently used, to be discontinued, in hospitals at least. Instead, the terms bacteriologist, biochemist, biophysicist, hæmatologist, histologist, or virologist could be used according to taste: each worker should have an individual laboratory, but all should be contiguous and in one central building, so having common meeting and stamping grounds. Medicine and pathology have both suffered enough enthusiastic divisionists already without further chemical schizists.

County Hospital, Lincoln. J. R. H. PINKERTON.

HYDROCORTISONE AND CORTICOTROPHIN IN HERPES ZOSTER

SIR,—During the past three months I have been using short courses of intensive hydrocortisone 10 mg. t.i.d. for four days in severe cases of herpes zoster—with dramatic results.

Severe pain is relieved in two days and herpetic vesicles seem to scab and separate at an earlier period. This has been particularly noticeable in severe herpes of the ophthalmic division of the 5th nerve. This treatment has also been used for herpes involving cutaneous branches of the brachial plexus, again with dramatic improvement.

I do not seem to have seen this reported elsewhere. The same improvement has been seen with the use of corticotrophin long-acting gel (40 units six-hourly for three days).

Rugby. J. A. WAKES MILLER.

VIRUS INFECTIONS DURING PREGNANCY

SIR,—I read your leader of Oct. 8 with much interest, because it fell to me to review this topic at the First International Conference on Congenital Malformations held in London in July, 1960.

May I take this opportunity to encourage those readers who may be continuing to investigate the outcome of rubella in pregnancy to arrange for the assistance of a laboratory where virus diagnostic tests can be performed?

Although the rubella virus has not yet been isolated—and we have had many negative results in Toronto—the Echo viruses that may cause a similar clinical syndrome can be readily grown in tissue culture.

Work done on the Echo viruses in Canada and many other parts of the world has convinced me that a diagnosis of "rubella" or "german measles" obtained from a patient must be considered unreliable. Even a physician may mistake infection with an Echo virus (especially type 9) for rubella. In differentiation, it is important to note the short incubation period of Echo infections (3–5 days).

Epidemiological studies such as those commented on in your editorial have produced substantial results. Such studies may, however, prove even more rewarding in the future when epidemiological techniques are correlated with the more precise laboratory techniques of the modern medical virologist.

School of Hygiene, University of Toronto. A. J. RHODES.

FATAL RESPIRATORY OBSTRUCTION DUE TO FAULTY ENDOTRACHEAL TUBE

SIR,—I have encountered this phenomenon of respiratory obstruction due to faulty endotracheal tube on three occasions. Simple deflation of the cuff has relieved the obstruction immediately, and the operation has been proceeded with. There is no need to change the tube.

A few weeks after my first case our registrar encountered this mishap, and deflation of the cuff again reversed a potentially serious position.

Morriston Hospital, Swansea. J. M. LEWIS.

HAZARDS OF BARIUM-SULPHATE ENEMA

SIR,—Your annotation of Oct. 8 refers to barium-sulphate pulmonary embolism. The following case may therefore be of interest as a record of a further hazard in relation to this common diagnostic procedure.

A fit man of 70 was referred from the outpatient department for barium enema. He complained of mucous diarrhœa. Technically the enema was uneventful. On walking from the X-ray table he complained of sudden severe abdominal pain and collapsed to the floor. The radiologist reported that he was unconscious for some seconds. He was transferred immediately to a general medical ward.

When examined he was conscious, complaining of generalised abdominal pain and mentioned a transient sharp left-sided chest pain. No peripheral pulses were detectable; blood-pressure was unrecordable and the jugular venous pressure was raised. It was then observed that a striking generalised erythema was developing: it reached a maximum some 45 minutes after completion of the enema, and faded gradually over the next 6 hours.

Immediate resuscitation was symptomatic, using oxygen, morphine, intravenous pressor agents, and intramuscular promethazine. Chest X-ray, plain X-ray of the abdomen, electrocardiogram, serum-transaminases, and urinary 5-hydroxy-indole-acetic acid were all subsequently shown to be normal. The barium enema showed a few diverticula in the sigmoid colon but no other abnormality. The patient made an uneventful recovery and was discharged 10 days later. The cause of his abdominal pain remains obscure.

In view of the negative findings and the clinical picture, this man may have had an acute hypersensitivity reaction The barium enema was made up in 1% tannic acid and was preceded by colonic irrigation with tap-water followed by 'Veripaque' enema. A similar investigation 4 months previously with the same preparation was entirely uneventful Skin tests using 1% tannic acid were negative.

Fatal collapse due to proven barium-sulphate pulmonary embolism has now been reported.[1] A second case in which this diagnosis seems highly probable, although necropsy was not allowed, has recently been recorded.[2] Acute "water intoxication" in the preparation of children for barium enema is now a well-recognised and sometimes fatal hazard.[3–5] But the condition I have described does not seem to have been recorded previously.

Over 1000 barium enemas are performed annually in this hospital; no member of the staff of the department of radiology has seen or heard of a similar case. Although,

1. Truemner, K. M., Vanlandingham, H. *J. Amer. med. Ass.* 1960, **173**, 1089.
2. Rosenberg, L. S., Fine, A. *Radiology*, 1959, **73**, 771.
3. Hiatt, R. B. *Ann. Surg.* 1951, **133**, 313.
4. Jolleys, A. *Brit. med. J.* 1952, i, 693.
5. *Lancet*, 1959, i, 559.

therefore, a most unusual event, its seriousness seems to warrant more general recognition. We are hoping to do further studies in an attempt to determine the nature and cause of this reaction. It would be interesting, meanwhile, to hear of any similar incident.

I should like to thank Dr. G. D. Hadley for his advice and permission to publish this case.

Middlesex Hospital, London, W.1. B. R. WEBSTER.

ACUTE COPPER POISONING

SIR,—The paper by Professor Semple and his colleagues (Sept. 24) is very timely, especially because the possibility of toxic hazards from copper heating vessels does not seem to be generally appreciated.[1]

It may be of interest to recall that Dr. Harold Jacobziner, assistant commissioner of the New York City Department of Health, commented last year on the toxic hazards of copper as well as other metals in hot tap-water drawn from corroded pipes lined by these metals.[2] He said that he had in his files "the report of an investigation of a case where several persons became ill due to excessive copper in water drawn from the bottom of a hot water tank". Jacobziner was commenting on a paper [3] which had recommended the use of hot tap-water in the preparation of infant feeds.

Memorial Hospital of Long Beach, Long Beach, California. GEORGE X. TRIMBLE.

ORAL TREATMENT OF PERNICIOUS ANÆMIA WITH LOW DOSES OF H.P.P./1

SIR,—Dr. Varadi (Oct. 15) must realise how increasingly difficult it has now become for us to assess the significance of his findings, faced as we are with three differing descriptions of the treatment given, and the responses obtained, from the same ten cases. It is also a matter of some surprise to find that he classifies a case as "relapsed" (Sept. 17) when, in fact, the patient did not suffer a deterioration in the blood-picture at all, but merely a fall in the serum-B_{12} level when the daily dose was reduced from 300 μg. to 100 μg. of B_{12}.

Finally, it is a little disappointing that Dr. Varadi has still declined to explain the scientific basis of his interpretation of serum-B_{12} levels, when applied to this particular form of therapy. We do not doubt that the estimation may be of some value in confirming a diagnosis in the untreated case of pernicious anæmia, but we would like to know what evidence he has for the conclusion in the penultimate paragraph of his letter of Sept. 17, that serum-B_{12} levels also reflect the degree of intestinal absorption, *on this particular form of therapy*.

F. S. MOONEY
St. Helens Hospital. J. G. HEATHCOTE.

SIR,—Like Dr. Varadi and Mr. Elwis (Sept. 17) I have been investigating the serum-vitamin-B_{12} levels of patients with pernicious anæmia in relapse who have been treated with vitamin-B_{12}/peptide ('Distivit').

In 8 such patients receiving 200 μg. daily or less, followed for periods of three to eighteen months, the serum-B_{12} concentration rose above 200 μμg. per ml. in 1 case only. A further 2 patients given 500 μg. daily for a period of eighteen months maintained serum levels around 400 μμg. per ml. These results are broadly similar to those previously reported [4] using oral crystalline vitamin B_{12}. With the exception of 1 patient receiving 100 μg. daily, all these cases reached and maintained normal values of hæmoglobin, red-cell counts, and packed-cell volumes, so Dr. Mooney and Dr. Heathcote (Oct. 1) could again, on this evidence alone, question the scientific basis for using serum-vitamin-B_{12} levels as proof of adequate dosage. I submit however that, as a general concept of rational therapy, it is desirable to give a sufficient amount of the vitamin to maintain the serum level near the average normal mean—that is, about 400 μμg. per ml. It therefore seems necessary, if oral treatment for pernicious anæmia is considered desirable for a particular patient, that over 200 μg. daily should be administered, whether the vitamin B_{12} is in a crystalline form or a peptide complex.

Coventry and Warwickshire Hospital, Coventry. N. K. SHINTON.

1. *J. Amer. med. Ass.* 1960, **174**, 550.
2. Jacobziner, H. *J. Pediat.* 1959, **55**, 797.
3. Fischer, C., Whitman, M. *ibid.* p. 116.
4. Marshall Chalmers, J. N., Shinton, N. K. *Lancet*, 1958, ii, 1298.

BROADER MEDICAL TEACHING

SIR,—May I comment on your interesting annotation Broader Medical Teaching (Oct. 22)?

On Oct. 23, 500 general practitioners attended our third *Medical World* Conference. One of the subjects was "Training for General Practice". From the discussion, several attitudes became apparent:

(*a*) The G.P.s agreed unanimously that their medical-school training had not fitted them for their work; (*b*) that, with few exceptions, hospital doctors who had trained them had little knowledge or understanding of the problems facing the G.P.; (*c*) that, despite a growing awareness of these deficiencies in training, the situation has not improved of recent years.

In a laudable attempt to correct an unbalanced system of training, some universities and the College of General Practitioners have introduced schemes to allow medical students to see something of general practice during their training. Apart from local schemes which allow students to spend a few weeks with selected G.P.s, there are the Edinburgh and Manchester University schemes. On a more ambitious scale the Inverness Regional Hospital Board is providing rotating internships, which include attachment to G.P.s, and the Wessex scheme financed by one of the Nuffield Trusts is seeking to provide young G.P.s with a chance to see something of all three branches of the Service.

No-one would wish to minimise these efforts. Yet surely they leave the main problem unsolved. The hospital teacher who will continue to form the minds of new generations of students is still out of touch with the problem of general practice. How can this be otherwise when the career structure in the hospital field demands that the young trainee consultant should unremittingly follow the narrow lines of his specialty?

I suggested at our conference that the problem could be partly solved if every future teacher in the hospital service had to spend a period in general practice—a proposal which was warmly welcomed. The time to do so would be between the registrar and senior-registrar appointments—i.e., before the young specialist sets his foot on the ladder from which he dare not fall off. If the time spent in general practice were made a condition of appointment to a senior-registrar post, no-one would gain an unfair advantage.

Unlike the G.P. trainees, these young aspiring specialists would not have to be taught general practice by selected good G.P.s. Their need is to see the realities of practice in all its forms. They could be attached to four different types of practice for six weeks each, and could learn quickly some of the problems facing the industrial, semi-urban, rural, and seaside G.P. In all, this would occupy only six months of their working lives, yet it could have a profound and beneficial effect on the future training of the medical student—and, indeed, on British medicine.

BRUCE CARDEW
London, W.C.1. Editor, *Medical World*.

Obituary

ALAN BROWN

M.D. Toronto, F.R.C.P.(C.), F.R.C.P.

Dr. Alan Brown was one of the pioneers of pædiatrics in Canada. For over thirty years he was physician-in-chief to the Hospital for Sick Children in Toronto, and when a chair of pædiatrics was set up in the University of Toronto in 1935 he was appointed the first professor. He died on Sept. 7 at the age of 73.

He qualified from the University of Toronto in 1909, and spent five years as a resident physician in the Babies' Hospital (Columbia University), New York. After further postgraduate study in Germany, Austria, Denmark, and Britain, he was appointed to the medical staff of the Hospital for Sick Children in Toronto in 1915. Four years later he became its physician-in-chief. Under his direction the hospital became a centre for the training of medical undergraduates, pædiatricians, and nurses. In 1919 he was appointed an associate professor of medicine in the university, and in 1935 head of the newly created department of pædiatrics. He served for many years as consultant to the local, provincial, and national departments of health, as well as to three other Toronto hospitals and the former Infants' Home. He was a founder and past president of the Canadian Pædiatric Society. He retired from his hospital appointments and his chair in 1951.

As a writer and a visitor he was well known on both sides of the Atlantic. His book on *The Normal Child*, first published in 1926, is now in its fifth edition, and with Dr. F. F. Tisdall he published a useful survey of *Common Procedures in the Practice of Pædiatrics*. He gave many clinical lectures, and his colleagues in this country will recall his Ingleby lectures in 1948 on the scientific construction of the normal child's diet. He was a corresponding member of the British Pædiatric Society and was elected F.R.C.P. in 1940.

E. C. R. writes:

"Alan Brown crusaded vigorously for many improvements in the care of infants and children, including the proper formulation and sterilisation of infant feedings, the compulsory pasteurisation of milk, and the universal use of diphtheria toxoid and other well-established immunisation procedures. Soon after he became physician-in-chief, he organised a small research laboratory at the hospital which, with his support and encouragement, has grown greatly with the years in both size and reputation. Canadian pædiatrics in general and the Hospital for Sick Children in particular owe a great deal to his vision, unusual energy, and outstanding organising ability."

Dr. Brown married Miss Constance Hobbs in 1914. She survives him with their two daughters.

CLAUDE WILFRED ALFRED KIMBELL

M.B. N.Z., F.R.C.O.G., F.R.C.S.E.

Mr. Claude Kimbell, gynæcological surgeon to the Samaritan Hospital for Women, London, died on Oct. 26 at the age of 55.

A New Zealander by birth, he was educated at Wellington College and the University of Otago, where he graduated M.B. in 1930. The following year he came to this country for postgraduate studies, and in 1935 he took the F.R.C.S.E. and in 1937 the M.R.C.O.G. During the late war he served in the R.A.M.C. with the rank of major. He remained behind at Dunkirk to look after the wounded and spent the rest of the war as a prisoner in Germany. Afterwards he returned to practise obstetrics and gynæcology in London and was appointed to the staff of the Samaritan Hospital and the City of London Maternity Hospital. He was elected F.R.C.O.G. in 1953. He was a founder member of the Gynæcological Travellers' Club.

C. M. G., one of his colleagues at the Samaritan Hospital, writes:

"Claude Kimbell was a sick man for many years, but because of his courage and interest in life he continued with his work. In the Samaritan Hospital he was loved by everyone he worked with in the outpatient department, wards, and theatre. An excellent surgeon, he was interested in the total human and always concerned with the psychological implications of a case. He was a perfectionist and ever ready to sacrifice himself for his patients and friends. From his experience as a prisoner-of-war he had learned not bitterness but a deep sympathy and understanding of his fellows."

J. H., who first met Kimbell twenty-five years ago on visits to Liverpool when Kimbell stayed with his fellow New Zealander, the late Charles Marshall, came to admire "his many qualities as friend and surgeon". He relates:

"Knowing that his health was failing Kimbell lately made a trip to Canada as a ship's surgeon to see his married daughter and grandchildren. In a Newfoundland hospital he found a sailor who had been seriously injured four months previously. No one would take the responsibility to send the sailor back to England and his family. It was typical of Claude Kimbell that he organised a passage home on his own ship for this injured man, and on arrival in Liverpool with great energy arranged for him to be sent home to his family.

"As a surgeon Kimbell was meticulous in detail and deft in technique. As a man I can sum him up in four words—modest, honest, generous, and always considerate of others."

Public Health

The Registrar General's Commentary

IN his commentary on the vital statistics for 1958 the Registrar General[1] notes that the birth-rate of 16·4 per 1000 was the highest recorded since 1949. There were 740,715 live births, the largest number since 1948. The birth-rate per 1000 women aged 15–44 was 82·1 in 1958, which was above the level of the early 1920s and 32% higher than the 1938 rate. The birth-rate was highest in Merseyside and lowest in Greater London.

Population.—The annual rate of increase amounted to about 0·5% of the population, a little less than the average rate of population increase for Northern and Western Europe, and only a third of the rate of increase in Asia. The estimated total population at mid-1958 was 45,244,000 (21,877,000 were males and 23,367,000 females).

Marriages.—In the 15–24 age-group, the proportion married has more than doubled since 1931 for both men and women. Although total marriages were 7000 less than in 1957, the rates continued to rise slightly at the younger ages. In 1954, 6·9% of bridegrooms and 28·6% of brides were minors; the corresponding figures for 1958 were 10·7% of bridegrooms and 35% of brides.

Deaths.—The crude death-rate—11·7 per 1000 persons of all ages—showed little change. With allowance for population age-changes, the average reduction in mortality has been 60% in the past fifty years, and 40% in the past twenty-five years. Between 15 and 24 years, the death-rate for males is more than double that for females; in this age-group seven times as many men as women die from accidents.

Infant mortality.—This continued to decrease: deaths of children under 1 year numbered 22·5 per 1000 births in 1958, the lowest rate recorded till then. Infant mortality as a whole has declined by two-thirds since 1928.

Tuberculosis.—There were 4480 deaths in 1958, compared with 19,797 in 1949. In the same time, annual notifications have declined from over 50,000 to 30,000.

1. Registrar General's Statistical Review of England and Wales, 1958: Part III, Commentary. H.M. Stationery Office. Pp. 222. 13s.

Accidental and violent deaths.—These have increased progressively, the totals being 18,513 in 1949 and 22,456 in 1958. The increase is due mostly to increases in motor-vehicle accidents, accidental gas-poisoning, falls, and, in women only, suicide. The death-rate among men in the 15–24 age-group from motor-vehicle accidents increased from 26 per 100,000 population in 1954 to 35 in 1958. Accidental deaths attributed to barbiturate poisoning increased from 77 in 1949 to 205 in 1958, and to domestic gas from 421 to 870.

The September Quarter

In England and Wales in the September quarter, 1960, there were 197,572 live births, 3873 stillbirths, and 112,379 deaths.[1] The birth-rate (17·2 per 1000 population) was the highest for a September quarter since 1948, when the corresponding rate was 17·5. The stillbirth-rate was low—19·2 per 1000 live and still births.

Parliament

Professions Supplementary to Medicine Bill

THIS Bill received the Royal Assent on Oct. 27. Its provisions will not come into operation until they are brought into force by Orders in Council.

QUESTION TIME

Hospital Casualty Services

Earl WINTERTON asked the Government whether, in view of the criticisms made by an unofficial committee of the methods for dealing with casualty cases in National Health Service hospitals and of other evidence to the same effect, they would appoint a committee of inquiry.—Lord ST. OSWALD replied: My Lords, the Standing Medical Advisory Committee of the Central Health Services Council appointed, earlier this year, a subcommittee, under the chairmanship of Sir Harry Platt, to consider the organisation of hospital casualty and accident services and to make recommendations regarding their future development. The Scottish Health Services Council has set up a similar committee. I have no doubt that these committees will consider the recommendations made in the study, based on 20 casualty departments, which was recently published for the Nuffield Provincial Hospitals Trust.

Lord STONHAM: Is the noble Lord aware that, at the instance of the Minister, every regional board has been considering this problem; that they are proposing to concentrate major casualty centres in the hospitals in each group, but that what is needed is more money to equip, expand, and provide more casualty centres? And can he say whether that will be forthcoming?—Lord ST. OSWALD: I think that any decisions of that nature must naturally rest upon the finding of this subcommittee, which has been set up specifically for the purpose of discovering what the facts are, and of suggesting remedies.

Means Test for State Scholarships

Mrs. EIRENE WHITE asked the Minister of Education what decision had been reached on the recommendations of the Anderson Committee on parental means tests for university students—Sir DAVID ECCLES replied: I shall very shortly announce a radical revision of the present means test, to be brought in by the autumn of 1961. This is without prejudice to the abolition of the means test if that, on full examination, should turn out to be required.

Smokeless Zones

On Oct. 1 there were 296 smokeless zones or smoke-control orders in operation in England and Wales, covering 255,974 premises, and 98 more smoke-control orders, covering 123,219 premises, have been confirmed but were not in operation. Some 1270 local authorities have not made smoke control orders, but most of these do not have a major problem of domestic smoke pollution.

1. Registrar General's Weekly Return, no. 42, 1960. H.M. Stationery Office. Pp. 204. 1*s*. 6*d*.

Notes and News

WORLD HEALTH ORGANISATION

THE Director-General of W.H.O., Dr. M. G. Candau, and the retiring senior W.H.O. representative in the Congo, Dr. J. S. MacKenzie Pollock, have both reported on the medical situation there.

In July W.H.O. responded to a request by the Security Council, and within a week 28 staff members had been sent to the Congo. 28 medical teams provided by 25 national Red Cross societies answered a joint appeal by the League of Red Cross Societies and the International Committee of the Red Cross. These teams were initially to stay three months. Some countries offered additional assistance; and soon hospitals, not only in the cities, but in the country as well, were able to function again.

At each provincial capital, except that of Katanga, there is a W.H.O. group, consisting of a public-health adviser, a public-health engineer, and a mobile epidemiological team. These mobile teams have already begun to organise vaccination campaigns against smallpox, typhoid fever, yellow fever, and plague. To deal with these diseases and the other major health hazards—malaria, filariasis, leprosy, and tuberculosis—many staff members are being recruited. They will be paid out of the U.N. Congo fund and placed at the disposal of the Congo Government. The main need is to staff the district services with doctors who will superintend the hospitals and organise preventive health services. 130 health personnel are being recruited now, and this number will soon be increased to about 500. The Red Cross teams have been asked to remain for six months, or longer if possible.

The long-term problems can be solved only by training Congolese doctors. There are none at present; and the local university, Lovanium, will graduate only 2 in 1961, and not more than 19 in all by 1965. Dr. Candau considers that the 1959 situation cannot be regained in less than twelve to fifteen years. But an encouraging start has been made. W.H.O. is providing 13 additional teaching staff, including the first professor of public health, which has enabled Lovanium University to increase its medical-student intake to 40. The three schools for "medical assistants" will finish the six-year training of the present students and then close. All students after that will complete the full medical course at Lovanium University. 74 "medical assistants" are at present helping to provide essential health services.

Meanwhile 60 "medical assistants" have been awarded W.H.O. fellowships and have left for French medical schools to qualify as doctors after special two-year or three-year courses. 7 students with no previous training have been awarded fellowships for a full medical course in France or Switzerland.

Dr. A. Bellerive (Haiti) succeeds Dr. McKenzie Pollock as senior W.H.O. representative.

In Geneva, the 26th session of the Executive Board opened on Oct. 25. Dr. Henrique M. Penido (Brazil) was elected chairman.

THE WORLD'S FOOD

"Food and population are two of the crucial determinants of the future of mankind. Freedom from hunger in the less developed countries of the world, however, is not simply a matter of regaining or maintaining pre-war levels of per caput production and consumption . . . Much greater increases in food production in these regions are needed before any real progress can be made in stamping out hunger and malnutrition. But increased food production must go hand in hand with general economic development so that consumers can afford the additional food and the better quality food they need."

In these words, taken from his foreword to F.A.O.'s latest annual report,[1] the Director-General summarises the agricultural problem confronting the greater part of the human race. While the highly developed countries continue to increase production (to the point of accumulating surpluses) by

1. The State of Food and Agriculture, 1960. F.A.O., Rome. Pp. 182. 10*s*. Obtainable from H.M. Stationery Office.

increasing yields, the increases in less developed countries have been mainly due to extension of cultivated areas: the abundance which would spring from the application of intensive methods of cultivation to these areas can only be imagined. The immediate problem is to provide enough food for the less fortunate. In the highly developed areas, not only has production increased but there has been growing emphasis on livestock; whereas in underdeveloped regions the modest increase in food production is imperilled by concentration on crops grown for sale. In Africa, for instance, there was actually a fall in food production in proportion to population: only coffee and cocoa showed large increases.

In the face of this urgent need, F.A.O. has undertaken to advise governments how to improve production. That this is not a simple matter of ploughs and fertilisers will be apparent to anyone who has read Gunnar Myrdal's excellent little book.[2] It is to be hoped that the highly developed countries will play their parts in this scheme: a guarantee of steady prices would be a boon to underdeveloped areas.

MEETING IN CZECHOSLOVAKIA

THE Czechoslovak Academy of Sciences has a great part to play in furthering the scientific integration of East and West. A small colloquium on developmental physiology with special reference to homœostasis was recently held at Liblice, an ancient castle near Prague belonging to the Academy, and brought together 33 scientists from Canada, Czechoslovakia, Great Britain, Hungary, the U.S.A., and the U.S.S.R. The meeting was very successful: the papers and discussions were most stimulating and the small numbers attending made it possible to get to know colleagues really well at informal meetings.

Papers were read by Prof. K. S. Koshtoyants, Prof. A. Ginetzinsky, Prof. V. N. Nikitin, and Prof. I. A. Arshavsky from Russia, Dr. E. F. Adolph and Dr. S. S. Chernick from the U.S.A., Dr. S. M. Friedman from Canada, Prof. E. Kerpel-Fronius from Hungary, and Prof. J. S. Heller, Prof. R. A. McCance and Dr. E. M. Widdowson, and Dr. L. E. Mount from Great Britain. A strong Czechoslovak representation included Prof. O. Poupa and Dr. J. Jelínek, Dr. K. Čapek, Dr. J. Křeček, Dr. I. Mikuláš, Dr. J. Martínek, Dr. M. Kraus, Dr. P. Hahn, Dr. O. Koldovský, and Dr. P. Fábry. Dr. E. F. Adolph (Chicago) was invited to take the chair.

Prof. A. Ginetzinsky (Leningrad) discussed the role of hyaluronidase in the control of urinary volume by the mature and immature kidney. Dr. S. M. Friedman (Edmonton) gave a stimulating account of his work on the relation between alterations in the concentration of sodium in the medium and the contractions of smooth muscle. Prof. J. S. Heller (Bristol) described his studies on species differences in the biochemistry of antidiuretic hormones and variations in their mode of action. Dr. K. Čapek (Prague) dealt with the development of transport mechanisms in the kidney and their sources of energy. Dr. O. Koldovský (Prague) showed how the absorption of glucose by young animals brought out the dangers of using a technique which might be reasonably satisfactory for an adult but is quite unsuitable for a newborn animal, even of the same species.

The participants were grateful for the warm hospitality of their hosts.

INTERNATIONAL BRAIN RESEARCH ORGANISATION

AN organisation, sponsored by UNESCO, has been set up to promote and coordinate basic research in all sciences involved in the study of the brain. Travelling fellowships will be awarded, working parties will consider special problems, support will be given to laboratories needing new premises and equipment for advanced teaching and research, travelling teams of instructors will supplement local teaching facilities, and expensive instruments will be made available to centres with limited resources. A census of research centres will be carried out and a directory compiled. Arranging conferences will be a minor activity since many other organisations already meet this need. The following branches of brain research are represented in the executive committee: anatomy, endocrinology, biochemistry, pharmacology, physiology, biophysics, and the behavioural sciences. Prof. H. H. Jasper (Montreal) has been elected executive secretary. The United Kingdom is represented on the committee by Prof. G. W. Harris. Details can be obtained from UNESCO, place de Fontenoy, Paris, 7e, France.

2. Myrdal, G. Economic Theory and Underdeveloped Regions. London, 1957.

FILM ON GERIATRIC REABLEMENT

New Beginnings [1] was filmed at the Lennard Hospital, Bromley, Kent, with Dr. Monnica Stewart as director.

The extent of reablement which can be achieved, even with limited facilities, is demonstrated by a patient, aged 73, admitted with right hemiplegia due to cerebral thrombosis. She is also obese and her knee on the unaffected side is arthrodesed. She is, however, very keen and cooperative, and gradually learns to wash herself again, get out of bed, dress, go up-stairs, and walk unaided.

The film underlines the need for teamwork by all concerned —doctors, nurses, occupational therapists, physiotherapists, ambulance drivers, members of the W.V.S., and others—to achieve such a result.

ABSTRACTS FROM JAPANESE JOURNALS

VERY few English-speaking doctors can read Japanese, and Japanese contributions to progress in medicine are thus inaccessible to most of them. The initiative of the Excerpta Medica Foundation in starting a monthly journal, *Abstracts of Japanese Medicine*,[2] will therefore be widely welcomed. The abstracts are selected from the weekly *Japanese Medical Abstracts* (*Igaku Chuo Zasshi*) by a Japanese editorial board. It is expected that between 5000 and 6000 abstracts, drawn from some 500 Japanese medical periodicals, will be published annually. The joint editors are Prof. T. Yoshida (Tokyo) and Dr. J. Huizinga (Amsterdam).

1. *New Beginnings*, made by the geriatric unit, Bromley Group Hospital Management Committee. Directed by Dr. Monnica C. Stewart. 16 mm. sound (optical track). Black and white. 40 minutes. Available on free loan from the Group Secretary, Bromley Group H.M.C., Farnborough Hospital, Farnborough, Kent.
2. *Abstracts of Japanese Medicine*, vol 1, no. 1. October, 1960. Obtainable from the Excerpta Medica Foundation, 56, Grosvenor Hill, London, W.1, or 119, Herengracht, Amsterdam C, Netherlands. £11 12s. per annum.

University of Cambridge

On Oct. 15 the following degrees were conferred:

M.Chir.—R. C. Shepherd.
M.B., B.Chir.—K. A. Macdonald-Smith, A. M. D. Mitchell (by proxy).
M.B.—M. I. J. Andrews, R. D. B. Leicester, P. R. C. Steele, J. P. Watson (by proxy).

University of London

Dr. Sydney Cohen has been appointed reader in immunology at St. Mary's Hospital Medical School.

University of Liverpool

A course for consultants in pædiatric anæsthesia is to be held from Nov. 7 to 12 at Alder Hey Children's Hospital and Royal Liverpool Children's Hospital. The visiting lecturer will be Dr. Robert Smith, of the Boston Children's Hospital.

University of Edinburgh

The following appointments have been made:

Dr. B. I. Davies, lecturer, department of bacteriology; Dr. C. M. Drillien, lecturer, department of child life and health; Dr. J. R. Sutherland, lecturer, department of medicine; Dr. D. C. Flenley, assistant, department of medicine; Dr. M. Jacobson, lecturer, department of physiology; Dr. W. E. S. Kiernan, lecturer, department of psychological medicine; and Dr. F. A. Boddy, assistant, department of public health and social medicine.

National University of Ireland

Dr. Éamonn de Valéra has been appointed professor of midwifery and gynæcology at University College, Dublin.

British Medical Association

Occupational Health Prize (£50).—Any member of the Association engaged in the practice of occupational health either whole-time or part-time is eligible for this prize. Entries must include personal observations and experiences collected by the candidates in the course of their work. Further particulars may be had from the secretary of the Association, Tavistock Square, London, W.C.1.

Royal College of Physicians of London

At a comitia on Oct. 27, with Sir Robert Platt, the president, in the chair, Dr. R. A. Hicling, Dr. Charles Newman, Dr. Desmond Curran, and Dr. J. F. Stokes were elected councillors and Sir Harold Boldero was re-elected representative on the committee of management. Dr. R. F. L. Logan was appointed Milroy lecturer for 1962. His subject will be the quality of medical care.

The following were elected to the membership:

B. G. Adams, M.B. Lond., W. L. Ashton, M.B. Lond., J. S. Cameron, M.B. Lond., M. L. Clark, M.B. Lond., G. C. Cook, M.B. Lond., R.A.M.C., Hilary J. Crawford, M.B. Lond., Theodore Crawford, M.D. Glasg., G. M. Davies, M.B. Cantab., John Dupré, B.M. Oxon., G. M. Edington, M.B.E., M.D. Glasg., S. D. Elek, M.D. Lond., H. J. L. Francis, M.B. Lond., M. P. Joyston-Bechal, B.M. Oxon., Saroj Kumari, M.B. Delhi, M. J. S. Langman, M.B. Lond., A. L. Maresky, M.B. Cape Town, Kekobad Minocher Mody, M.D. Bombay, R. M. Norris, M.B. N.Z., N. W. Oakley, M.B. Cantab., D. O. Oliver, M.B. N.Z., Chinganezhath Krishnan Ramachandran, M.B. Madras, Ellen L. M. Rhodes, M.B. Leeds, J. F. Robinson, M.B. Lond., R. S. C. Scoular, M.B. N.Z., Leonard Sinclair, M.B. Lond., A. D. M. Smith, M.B. Wales, Peter Stephenson, M.B. W'srand, D. J. Ward, M.B. St. And., P. S. W. Wilkins, M.B. Birm.

Licences to practise were conferred on the following, who have passed the final examination of the Conjoint Board:

Makendra Krishnlal Vithaldas Adalja, R. O. Addae, Adeoye Adeniyi, F. P. Adler, Andani Andan, Peter Anderson, A. F. J. Atkins, J. C. C. Ayling, Margaret L. Birtwistle, Shirley M. Blackman, Iain H. Blair, Waalko Joost Boerema, Shirley A. Bond, H. C. Booth, G. T. Bowra, A. J. Bron, Catherine M. L. Brown, H. M. Carpenter, T. I. Cash, M. E. Cavendish, B. Wan-Bun Chan, Hung Cheng, T. J. H. Clark, Pauline T. Combe, K. J. Connolly, Kathleen Curtis, R. S. Dawkins, M. J. Denham, I. S. Duff, Elizabeth A. Edwards, P. R. M. Ernst, P. R. Evans, P. R. H. Evison, Gillian Freeman, Wilfred Galley, A. E. Gent, J. D. Gibling, David Glatt, Vasudeo Laxmanrao Gokhale, R. W. D. Gomes, C. D. Granger, D. G. Gwyn, George Hamber, John Hamilton-Paterson, Josephine E. Hammond, R. I. Harrison, Judith M. Hawker, J. B. Hicks, Amir Himaya, James Holmes, John Hood, A. P. Hopkins, Joan N. Horton, D. P. M. Howells, G. V. Hughes, P. M. Humberstone, D. M. Hunter, Jamil Menashi Ibrahim, E. G. Jackson, D. C. Jeffery, G. J. Johnson, M. T. Jones, P. N. Kersley, David King, Kwamena Kyei-Mensah, T. R. Lawson, Eveline B. McCulley, A. F. McGibbon, R. K. Mackenzie-Ross, I. C. McLellan, K. M. A. Madgwick, M. P. Madigan, J. R. Mansfield, P. H. Millard, N. D. Minton, John Moore, Ursula V. L. Morris, P. B. Mudge, J. F. O. A. I. Mustaffah, Margaret A. Nunan, C. S. Ogg, N. N. V. O'Sullivan, Dinesh Jayantilal Patel, P. B. Pattison, R. H. Pearce, E. P. Pereira, Mary Petrelli, Edward Proctor, Jacqueline J. Rees, Sankar Sahai, Wendy D. Savage, Jean A. Skinner, C. J. Spivey, J. D. Swales, F. J. B. Taylor, William Thompson, Sheila M. Thwaites, P. E. Walker, E. R. Walrond, L. M. Webber, M. M. Wicks, J. G. Woolich, J. S. C. Wright, F. W. Yates, F. M. Young, Ting Chiu Yu, W. W. Zadron.

Postgraduate diplomas were conferred on those named in the report of the Royal College of Surgeons in our issue of Oct. 22 (p. 937) and on the following:

D.C.H.—Pushpa Lal Rajbhandari.
D.P.M.—J. B. Collinson.

$1 million for Medical Research

The Times (Oct. 31) announces that Mr. Garfield Weston has given $1 million (about £357,000) to the Banting-Best department of medical research in the University of Toronto.

College of General Practitioners

Dr. Lindsey Batten will give a James Mackenzie lecture on Saturday, Nov. 19, at 11.30 A.M., at B.M.A. House, Tavistock Square, London, W.C.1. His subject will be The Medical Adviser.

British Association in Forensic Medicine

A meeting of this Association will be held on Saturday, Nov. 26, at 10.30 A.M., at St. George's Hospital, London, S.W.1, when there will be a symposium on patterns of injury.

Association of Surgeons of Great Britain and Ireland

The annual meeting of this Association will be held in Bristol from April 6 to 8. The programme will include discussions on organ transplantation and on trauma.

Westminster Medical School

Dr. J. J. Bunim, of the National Institutes of Health in Bethesda, is to give a lecture at the school, Horseferry Road, S.W.1, on Wednesday, Nov. 30, at 5.30 P.M. His subject will be the Interrelationships of the Collagen Disorders.

Industrial Welfare Society

This society, with the Nuffield department of occupational health at Manchester University, will hold a conference on industrial health at the Industrial Gas Development Centre, Whitworth Street West, Manchester, on Thursday, Nov. 17, at 10 A.M.

Release of Corticotrophin

Corticotrophin will be generally prescribable by doctors in Great Britain and Northern Ireland from Dec. 1.

Metropolitan Ear, Nose and Throat Hospital

On Tuesday, Nov. 8, at 5.30 P.M., at Rushcliffe House, St. Mary Abbots Hospital, Marloes Road, London, W.8, Mr. R. Scott Stevenson will give a lecture on vertigo.

Hand Clubs

A meeting of these clubs is to be held on Saturday, Nov. 19, at 10 A.M., at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2, under the presidency of Mr. Patrick Clarkson. The programme will include discussions on modern principles and techniques in the treatment of hand fractures and on operative treatment of Dupuytren's contracture.

Medical Research Council

The Council have set up a Gastroenterology Research Unit, under the direction of Dr. E. N. Rowlands, at the Central Middlesex Hospital; and a Unit for Research on the Chemical Pathology of Mental Disorders, under the honorary direction of Prof. I. E. Bush, in the department of physiology at Birmingham University.

Institute of Education

Dr. Nicolas Malleson has been appointed director of the new research unit for student problems at the University of London Institute of Education. The unit will undertake and foster sociological and operational research into problems of student performance and student life in the university generally.

Empire Rheumatism Council

This Council has set up an electron microscopy unit under the direction of Prof. D. V. Davies at St. Thomas' Hospital Medical School. Research workers in rheumatology who wish to have access to an electron microscope should apply to the Council, Faraday House, 8, Charing Cross Road, London, W.C.2.

Agricultural Research Council

The following appointments have been made at the Council's Institute of Animal Physiology at Babraham, near Cambridge:

Dr. Richard Keynes, head of the physiology department (in succession to Dr. I. de Burgh Daly); Dr. Catherine Hebb, head of a subdepartment of chemical physiology; Dr. Theodore Gillman, head of the experimental pathology department (in succession to Sir Alan Drury); Dr. G. D. Greville, head of the biochemistry department (in succession to Sir Rudolph Peters); Dr. Marthe Vogt, head of a new pharmacology unit. As already announced, Dr. J. H. Gaddum has succeeded Dr. de Burgh Daly as director.

The Wellcome Trust

Grants totalling over £240,000 were made by the Trust during the half-year ended Aug. 31. They included:

Middlesex Hospital Medical School, London.—£50,000 for a suite of Wellcome research laboratories in the pharmacology department of the new medical school building.

* *Massachusetts General Hospital, Boston, U.S.A.*—£50,000 to establish a Wellcome research professorship for ten years.

Medical Research Council.—£61,000 to construct a laboratory and housing accommodation for an epidemiological research unit in Jamaica.

* *Medical Research Council.*—£60,000 to provide five Sir Henry Wellcome research travelling fellowships for five years.

McGill University, Montreal, Canada.—£40,000 to extend the support of the Wellcome research department of anæsthesia for a further five years.

University of Pennsylvania, Philadelphia, U.S.A.—£17,000 to extend the support of the Wellcome associate professorship of research in anæsthesiology for a further three years.

Trinity College, Dublin.—£16,000 to construct and equip an experimental surgery unit and an animal house.

Oxford University.—£16,300 to construct an animal house for the use of workers in the department of the regius professor of medicine.

Postgraduate Medical School, London.—£6,000 to equip a cardiac catheterisation research laboratory in the department of medicine.

Department of biochemistry, University of Birmingham.—£10,000 for equipment to study the nature and functions of the proteins of brain and muscle.

St. Mary's Hospital Medical School, London.—£8500 for an analytical ultracentrifuge to study the structure of antigens and antibodies.

Research Apparatus.—Grants (totalling £21,800) were made to Prof. Ronald Woolmer, Dr. G. A. Kerkut, Mr. H. A. Sissons, Dr. K. S. Dodgson, Prof. O. L. Wade, Prof. G. A. H. Buttle, Prof. J. W. Howie, and Prof. J. H. S. Heller. A grant (£1000) to purchase equipment for high-altitude research was made to Dr. L. G. C. E. Pugh.

* Already announced.

A Medical Staff Residence

On Oct. 18, at Odstock Hospital, Salisbury, a new residence for medical staff was officially opened by Mr. P. G. Templeman, chairman of the Wessex Regional Hospital Board.

The residence has 17 bed-sitting-rooms each with its own wash-hand basin and built-in furniture. A large lounge is separated from the dining-room by sliding doors and meals are served from a small service kitchen adjoining the dining-room. There is a library away from the living-room area. Two flats for married residents have been built beside the new residence. The flats are furnished and centrally heated, and each has a lounge/dining-room, kitchen, main bedroom, and spare room. The cost of the whole scheme, including furnishings, was £35,000.

Award for Medical Film

La Presse Médicale is again offering a prize (1000 NF) for a medical 16 mm. film whose time of projection does not exceed 30 minutes. Films should be sent to the journal, 120, boulevard Saint-Germain, Paris VI[e], before Feb. 1.

Calorie Balance in Man

The Nutrition Society is to hold a symposium on this subject on Saturday, Dec. 17, at the Middlesex Hospital Medical School, London, W.1. The speakers will be Dr. J. V. G. A. Durnin, Dr. O. G. Edholm, Dr. Raymond Greene, Dr. T. M. Chalmers, Dr. G. C. Kennedy, Dr. A. M. Thomson, Dr. F. E. Hytten, and Dr. E. M. Widdowson. Further particulars may be had from the hon. programmes secretary of the society, Miss D. F. Hollingsworth, c/o Ministry of Agriculture, Fisheries and Food, Great Westminster House, Horseferry Road, S.W.1.

A meeting of the Biochemical Society is to be held on Friday, Nov. 18, at 10 A.M., at the Middlesex Hospital Medical School, London, W.1, when there will be a colloquium on histochemistry.

Professor J. B. Duguid, who has lately retired from the chair of pathology in the University of Durham, has left for Malaya, where he is to be an adviser in histopathology under the Technical Cooperation Scheme of the Colombo Plan.

The Association of Universities of the British Commonwealth (36, Gordon Square, London, W.C.1) have published a list of fellowships, scholarships, and grants tenable at universities in the United Kingdom and a short list of awards tenable outside the United Kingdom. Copies are being sent to universities and libraries and to other institutions on request.

A committee meeting of the Group for Representation of the Views of Clinical Psychiatrists will be held on Thursday, Nov. 10, at 5.30 P.M., at Tavistock House North, Tavistock Square, London, W.C.1.

The London Medical Exhibition will be held in the New Hall of the Royal Horticultural Society, Westminster, from Nov. 14 to 18.

University College London will hold a reunion dinner at the college on Friday, Feb. 17, for undergraduates or postgraduates who entered before 1918. Early applications for invitations should be made to the assistant secretary of the college, Gower Street, W.C.1.

From Nov. 21 the address of the National Council for the Unmarried Mother and Her Child will be 255, Kentish Town Road, London, N.W.5.

Film about Handicapped Children—The Cine Club of Bristol, with the help of the South Western Regional Hospital Board and the Bristol education and health committees, has produced *Claremont*, which shows how children with spastic disabilities are educated and treated at a school at Claremont, Bristol. The film, which is in 16 mm. colour, has a sound commentary and lasts about 12 minutes. The hiring fee is 1 guinea. Applications should be sent to the medical officer of health, central health clinic, Tower Hill, Bristol, 2.

CORRIGENDUM: *Treatment of Urticaria.*—The dose of proguanil ('Paludrine') mentioned in Sir Charles Dodds' letter of Oct. 22 should have been 0·1 g. (100 mg.).

Diary of the Week

NOV. 6 TO 12

Monday, 7th

POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12
4 P.M. Dr. Brian Ackner: Diagnosis of Depressive Illness.

Tuesday, 8th

UNIVERSITY OF LONDON
5 P.M. (London Hospital Medical College, Turner Street, E.1.) Dr. Preston A. Wade (Cornell University): Recent Advances in Fracture and Accident Services.
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.30 P.M. *Experimental Medicine and Therapeutics.* Dr. A. J. Buller, Dr. O. C. J. Lippold: Normal and Abnormal Willed Movement.
8 P.M. *Psychiatry.* Dr. J. J. O'Dwyer, Dr. Elliott Jaques: Use of Psychiatric Skills in Industrial Organisations.
BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Dr. W. M. Court Brown: Chromosome Analysis and Clinical Medicine.
ST. MARY'S HOSPITAL MEDICAL SCHOOL, W.2
5 P.M. (Wright-Fleming Institute.) Mr. D. G. Bonham: Non-malignant Enlargement of the Ovary.
INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. O. L. S. Scott: Anomalies of Pigmentation.
MANCHESTER MEDICAL SOCIETY
8 P.M. (Clinical Sciences Building, York Place.) *Surgery.* Mr. Ambrose Jolleys: Treatment of Peripheral Tuberculous Glands. Dr. H. B. Andrews: Tuberculous Glands.
LEEDS NEUROLOGICAL SCIENCES COLLOQUIUM
5.15 P.M. (General Infirmary at Leeds.) Dr. Paul Sandifer: Involuntary Movements in Children.

Wednesday, 9th

UNIVERSITY OF LONDON
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. Charles Wilcocks: Aspects of Medical Investigation in Africa—Trypanosomiasis. (Third Heath Clark lecture.)
POSTGRADUATE MEDICAL SCHOOL
2 P.M. Dr. P. J. Rendle: Regulation of Carbohydrate Metabolism by Hormones and Other Factors.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. Henry Haber: Skin Cancer.
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. Paul Wood: Present Position of Anticoagulant Therapy.
MANCHESTER MEDICAL SOCIETY
5 P.M. (Medical School, University of Manchester.) *Pathology.* Dr. Leon Poller: Pathogenesis of Thrombosis.
UNIVERSITY OF LEEDS
5 P.M. (General Infirmary at Leeds.) Miss U. M. Lister: Placenta.
6 P.M. Mr. T. F. Redman: Inefficient Uterine Action.
ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH, 9, Queen Street, Edinburgh.
5 P.M. Lord Cohen of Birkenhead: Changing Concepts of "Diathesis" in Medicine. (Frederick Price lecture.)

Thursday, 10th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Dr. Wade: Accident Surgery of Motorways. (Watson-Jones lecture.)
UNIVERSITY OF LONDON
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. Wilcocks: Aspects of Medical Investigation in Africa—Implications. (Last Heath Clark lecture.)
ROYAL SOCIETY OF MEDICINE
5 P.M. *Ophthalmology* and *Dermatology.* Dr. G. B. Dowling, Dr. J. A. Dudgeon, Mr. E. S. Perkins: Behcet's Disease. Dr. I. B. Sneddon, Mr. Barrie Jones, Mr. Frederick Ridley, Sir Benjamin Rycroft: Bullous Conditions of the Skin and Conjunctiva.
BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. M. R. Pollock: Physiological Adaptation in Micro-organisms.
ALFRED ADLER MEDICAL SOCIETY
8 P.M. (11, Chandos Street, W.1.) Mr. Lewis Way: Problems of Social Psychology.
CECIL GORDON LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Prof. Lancelot Hogben: Nature-Nurture Issue and the Medical Curriculum.
HONYMAN GILLESPIE LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Mr. J. H. S. Scott: Accident Services.
UNIVERSITY OF ST. ANDREWS
5 P.M. (Physiology Department, Queen's College, Dundee.) Prof. M. F. A. Woodruff: Outlook for Transplantation of the Kidney in Man.

Friday, 11th

POSTGRADUATE MEDICAL SCHOOL
10 A.M. Mr. A. J. C. Latchmore: Surgery of the Biliary Tract.
4 P.M. Prof. W. S. Peart: Ischæmic Kidneys in Hypertension.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
3.30 P.M. Dr. D. A. Osborn: Disorders of the Blood in E.N.T. Practice.

Appointments

BOYD, J. M., M.B. Glasg., D.P.H.; depute M.O.H., Renfrewshire.
DARLOW, A. R., M.B. Lond., D.P.H., D.C.H., D.T.M. & H.: divisional M.O., Bedfordshire.
GRAHAM, P. A., M.B. Glasg., F.R.C.S.: consultant ophthalmologist, United Cardiff Hospitals and Welsh Regional Board Hospitals.
HAINES, CICELY R., M.B. Sheff., D.OBST.: assistant M.O.H. and school M.O., Bournemouth.
SPENCER, P. M., M.B. Lond., F.R.C.S., M.R.C.O.G., D.OBST.: consultant obstetrician and gynæcologist, Elizabeth Garrett Anderson Hospital, London.
THOMPSON, R. B., M.D. Durh., M.R.C.P.: consultant physician, Royal Victoria Infirmary, Newcastle upon Tyne.
TURNER-WARWICK, MARGARET E. N., D.M. Oxon., M.R.C.P.: consultant general physician, Elizabeth Garrett Anderson Hospital, London.
WRIGHT, D. G., M.B. Glasg., F.R.C.S.E.: consultant orthopædic surgeon, Durham group of hospitals.

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